The Journal of Allergy

VOL. 17 JANUARY, 1946 No. 1

American Academy of Allergy

First Annual Meeting, New York, N. Y., Dec. 11 and 12, 1944

(Concluded)

STUDIES ON POISON IVY AND OTHER DERMATITIS-PRODUCING PLANT PARTS WHEREIN ACTIVE, RESINOUS PRINCIPLES ARE SUSPENDED IN AQUEOUS SOLUTION*†

MARGARET B. STRAUSS, M.S., AND W. C. SPAIN, M.D., NEW YORK, N. Y.

IT IS known that oleoresinous substances which cause a contact dermatitis in susceptible individuals can be obtained from the leaves of poison ivy, poison oak, poison sumac, and primrose by treatment with methanol, ethanol, toluene, petroleum ether, or diethyl ether. These oleoresins are known to be composed of a solution of acidic resins in essential oils.

Many attempts have been made to isolate the active component of the ivy plant in pure form. Pfaff,[1] in 1897, isolated a very toxic, nonvolatile oil, toxicodendrol. Acree and Syne[2] obtained a glucoside, toxicodendrin, and McNair[3] thought that the poison was lubinol, an unsaturated o-dihydroxy benzene derivative. Majima[4] obtained a toxic, relatively nonvolatile oil from *Rhus vernicifera* called urushiol, which was believed to contain an o-dihydroxy benzene having a normal fifteen carbon atom substituent in the 3-position. Hill and his coworkers[5] confirmed the above structure of urushiol and also reported that it was very toxic and caused the characteristic dermatitis of poison ivy. Mason and Schwartz,[6] following Hill's method, obtained three toxic oily fractions and reported that 0.5 γ of the oil per square centimeter of hypersensitive skin was sufficient to elicit a strong reaction characteristic of poison ivy. A compound related in molecular structure, 3-geranyl catechol, was shown by Landsteiner and Jacobs[7] to give positive tests on animals sensitized with urushiol, and Keil[8] obtained positive skin tests when 3-geranyl catechol was applied as a 1 per cent solution. From these reported observations it seems likely that more than one toxic compound present in the ivy plant causes dermatitis venenata. Therefore, it would seem desirable at the present time to continue use of compositions containing active principles of the entire leaf for phylactic and prophylactic treatment in immunization against poison ivy, poison oak, poison sumac, primrose, and the like.

*From the Allergy Laboratory, Department of Medicine, New York Post-Graduate Medical School and Hospital, Columbia University, New York.

†Read before the First Annual Meeting of the American Academy of Allergy, New York, Dec. 11, 1944.

The poison ivy extracts available at the present time for testing or treatment of sensitive individuals by the parenteral route consist of a solution of the oleoresin in alcohol as proposed by Spain and Cooke[9] or in an oil such as almond,[10] corn,[11] peanut, or sesame. Each of these extracts is somewhat unsatisfactory for general use because each requires extra care in handling and administration. For example, when administering the resinous extracts in which the active principle is dissolved in oil, it is necessary to make a deep injection (intramuscular) with a relatively long, thick needle (1 to 1½ inches long; 18 to 20 gauge) for, when a finer needle is used, the oily solution cannot be drawn into the syringe or delivered.[12] Furthermore, the syringes and needles are much more difficult to cleanse after use with oil extracts than after use with an aqueous solution. A still further disadvantage incident to use of the oil extracts is that, when administered intramuscularly, they often cause pain, and the presence of minute quantities of protein in the oil, especially when peanut oil is used, can cause severe reactions in an allergic individual. The alcoholic resinous extracts in general use consist of the active oleoresinous material dissolved in ethanol (95 to 100 per cent). Traces of water in these extracts cause rapid deterioration[9]; hence, when withdrawing a portion of extract from the stock container, exceptional care must be exercised so that no water enters the container from the syringe or needle used. In addition to the need for these precautions, use of the alcoholic extracts is troublesome because strongly alcoholic solutions cannot be injected due to the great pain and local tissue irritation which results. Accordingly, these extracts must be diluted, preferably with saline solution, immediately before use; and even after dilution these preparations still produce pain as they contain from 5 to 10 per cent alcohol.

The studies herewith reported, which were undertaken to provide new allergenic substances which would be free from the afore-mentioned disadvantages of previously known materials, were based upon the concept that an "extract" containing the active oleoresins or principles of poison ivy, poison oak, poison sumac, primrose, or the like in an aqueous medium would possess novel and desirable characteristics.

Shelmire[13] attempted to make water extracts of the ivy plants by directly extracting plant parts with aqueous solutions, but these extracts, although having some initial activity, wholly lost this activity in from one month to six weeks. Shelmire[14] later showed that the oleoresin obtained by treatment of the plant parts with ether, when initially dried and then allowed to stand in contact with water for many months, exhibited only slightly reduced activity when the oleoresin was dissolved in ether or acetone and the solution was tested on sensitive persons. This result can be contrasted to Spain and Cooke's observation (that traces of water caused deterioration of an alcoholic solution of ivy oleoresin) upon the basis that, in the latter instance, the ivy oleoresin was dissolved in an alcohol-water mixture, whereas, in the former instance, the insoluble dried oleoresin was merely in contact with the water.

In the course of the present investigation experiments were devised in which the active principle of the ivy plant could be obtained as a relatively insoluble stable precipitate from an aqueous solution.

In general, the method consists initially of extracting the plant leaf with pyridine. Pyridine, a weakly basic tertiary amine, is an unsaturated heterocyclic organic compound consisting of five carbon atoms, one nitrogen atom, and hydrogen; it is a liquid which is miscible with water. It is relatively nontoxic and is known to possess antispasmotic and antiseptic properties, a 10 per cent solution having been used by atomizer in treatment of asthma.[15, 16]

When the pyridine is initially added to the ground leaves minute bubbles of gas, formed on the surface of the solid material and apparently due to a reaction between the pyridine and the leaves, are evolved. It is considered likely that a reaction product between pyridine and the allergenic principle in the plant part, such as a complex of the type of a quarternary pyridinium salt, is formed.

The pyridine plant leaf "extract" thus obtained, which contains the active oleoresinous material capable of producing contact dermatitis on susceptible individuals, is then removed from the leaves and mixed with water; then the active material is precipitated by addition of a solution containing at least one of the substances of the class consisting of aqueous mineral acids, aqueous alkalis, and aqueous alum. The precipitate formed is removed by filtering or centrifuging, is washed repeatedly with water, and is suspended with isotonic saline solution.

Various other materials have been tested in this process as a substitute for pyridine; these materials include both unrelated organic compounds miscible with water (such as ethyl alcohol, acetone, isopropyl alcohol, and propylene glycol) and also related compounds such as the unsaturated tertiary amine, quinoline, the saturated secondary amine, piperidine, triethanolamine, and triethylamine. All of these unrelated organic compounds were found to be unsatisfactory because only very small amounts of precipitate were obtained after the addition of alum and/or the precipitate became oily on standing, becoming incapable of being satisfactorily dispersed in the aqueous solution and tending to stick to the container. As to the related compounds, the piperidine-ivy complex yielded only a slight precipitate on prolonged treatment with potassium alum solution which was not comparable to the yield obtained by use of pyridine. In experiments using quinoline, because of its relatively slight solubility in water, the quinoline-ivy complex was mixed with acetone prior to dilution with water, and then the active principle was precipitated as previously described. The precipitate, which was obtained in good yield, on subsequent washing agglomerated to form an oily mass which was difficult to suspend in saline solution. In like manner but different degree, triethanolamine, triethylamine, aniline, and dimethyl aniline were found to be unsatisfactory for use in the new procedure herein described. From these observations, it is now tentatively postulated that a heterocyclic tertiary amine is essential for satisfactory operation according to this procedure inasmuch as piperidine (which is a saturated pyridine and a secondary amine) gave very poor results; triethanolamine and triethylamine (aliphatic tertiary amines) did not yield the desired alum precipitates; and quinoline (a tertiary amine) gave a product far superior to any of the other products except that obtained with pyridine.

Although experiments with this new process indicate that the aqueous alum solution or the acid-alum solution are superior to other reagents for precipitating the active principles, other reagents can be employed if desirable inasmuch as aqueous mineral acid solutions or aqueous alkali solutions can cause formation of an active precipitate. When hydrochloric, sulfuric, or phosphoric acid or the like is used to cause formation of the active poison ivy precipitates from an aqueous pyridine-poison ivy "extract," the products tend to form oily agglomerates upon standing. When the alum solution is used, however, maximum precipitation is obtained and, even more important, the alum precipitate is finely divided and thus is superior to that obtained by precipitation with acid or alkali solutions. However, it is found that the addition of a small quantity of acid to the alum solution allows use of a smaller amount of alum without affecting the product.

It is possible to treat the deep green pyridine-ivy "extract" with fullers' earth or other such adsorbents to remove a large amount of chlorophyll, but, since a certain amount of active material is also adsorbed and lost, this has never seemed a worth-while refinement in the procedure.

All of the experiments reported herein, including those upon human beings and other animals, utilized an alum precipitated pyridine-ivy complex made as follows. The ivy leaves were treated with pyridine and, after diluting with water, the active principle was precipitated by addition of an aqueous alum solution or, in certain experiments, by use of an acidic aqueous alum solution.

PROCEDURE

Fresh leaves are dried in an oven at 40 to 50° C. until the leaves are brittle but still retain their dark green color. The dried leaves are passed through a sieve to remove the stems and midribs or, if preferred, the fresh leaves are passed through a grinder.

Another modification of the procedure can include extracting the freshly harvested ground leaves when received without preliminary drying.

1. *Procedure Starting With Dried Leaves.*—Ten grams of the dried plant leaves are added to 100 ml. of pyridine. This mixture is allowed to stand for twenty-four hours at room temperature and then is filtered. This stock solution of the pyridine complex, which is a deep green color, is stored in corked bottles and is autosterilized. The next steps in the procedure are preferably performed in a 200 ml. capacity Pyrex centrifuge cup (etched at the 40 ml. level). In this manner, the precipitation, centrifugation, washing, and dilution to final volume are completed in a single container.

Into a sterile 200 ml. Pyrex centrifuge cup containing 108 ml. of sterile distilled water, 40 ml. of the previously described stock solution are introduced with a sterile pipette. The solution is thoroughly mixed and, immediately thereafter, 32 ml. of a sterile solution of 5 per cent potassium alum by weight are added dropwise with continuous agitation. If an acid-alum solution is to be employed, the following proportions can be used in the same manner: 100 ml. of distilled water, 40 ml. of the afore-described stock solution and, 40 ml. of

0.25 N. sulfuric acid solution containing potassium alum, 2 per cent by weight. In each instance, a voluminous, finely divided, deep green precipitate is formed. The centrifuge cup is covered and the mixture is allowed to stand for twenty-four hours at 5° C.; then the mixture is centrifuged and the clear supernatant fluid is removed and discarded. The cup containing the residue is then filled with 200 ml. of sterile normal saline containing 0.4 per cent phenol and the precipitate is thoroughly mixed with this solution. The mixture is centrifuged, and again the supernatant wash solution is removed. This procedure is further twice repeated. After the last supernatant liquid has been removed, sterile saline is added to a total volume of 40 ml., the mixture is stored, and it is then transferred to sterile vials stoppered with sterile rubber caps. It will be noticed that the volume of the final product is equal to the volume of the stock solution originally used; thus, the former is approximately comparable to Spain and Cooke's[9] concentrated stock solution. However, these two types of solution may not be comparatively tested with an oily (corn) ivy extract, since the last is diluted on the basis of the weight of resinous material extracted with ether and the first two are diluted on the basis of the weight of the originally extracted dried leaf.

2. *Procedure Starting With Fresh Leaves.*—When fresh leaves are extracted, the water content is taken into account so that the same proportion of potassium alum to dried leaf is maintained as is in the procedure starting with dried leaves. About 10 Gm. of fresh leaves of poison ivy, poison oak, and poison sumac are approximately equivalent to 3.5 Gm. of dried leaves; 10 Gm. of fresh primrose leaves are approximately equivalent to only 1.5 Gm. of dried leaves.

About 10 Gm. of fresh ground leaves (poison ivy, poison oak, and poison sumac) are added to 100 ml. of pyridine. This mixture is allowed to stand at room temperature for twenty-four hours and is then filtered. The pyridine-fresh plant leaf complex is the stock solution from which the new antigenic product is obtained. Into a sterile centrifuge cup containing about 100 ml. of sterile distilled water, 114 ml. of this stock solution (of poison ivy, poison oak, and poison sumac) are introduced with a sterile pipette. The solution is mixed, and immediately thereafter 40 ml. of a sterile 0.25 N. sulfuric acid solution containing 2 per cent potassium alum by weight are added dropwise with continuous agitation. In each instance a voluminous, finely divided, deep green precipitate is formed. Alum solution alone as described previously may also be used. This mixture is further processed as described in Procedure 1 for the dried leaf extract and yields a product similar to that therein described.

Larger quantities of fresh leaves, such as 20 Gm., may be added to 100 ml. of pyridine. The same procedure is followed as outlined except that less stock solution is used in the precipitation of the active complex. To 100 ml. of sterile distilled water are added 57 ml. of the pyridine-fresh leaf stock solution. This solution is further processed as in the preceding procedure and yields a product similar to that therein described.

3. *Pollen Oil.*—By extraction of plant parts, such as the pollen, with ethyl ether, petroleum ether, toluene, and benzene, oils and resins are obtained and were shown by Stull, Cooke, and Chobot[17] to be nitrogen-free. The pollen oils

contain none of the antigenic activity associated with (1) hay fever which is due to an inhalant allergen or (2) the aqueous protein extracts which give positive intracutaneous tests on hypersensitive individuals but are responsible for the dermatitis which occurs on the skin of hypersensitive persons due to contact with the oil. The pollen oils are, at present, available as an alcoholic extract, but it is possible to suspend the active principle of the pollen oils in aqueous solution in the same manner as has been described for the plant leaves.

The pollen oil and resin are obtained by extracting the pollen with ethyl ether, filtering the mixture, and then removing the ether by evaporation at room temperature. About 2 Gm. of pollen oil are then added to 100 ml. of pyridine. Into a sterile centrifuge cup containing 100 ml. of sterile distilled water are added 40 ml. of the pyridine-pollen oil stock solution and then, after mixing, 32 ml. of a solution of 5 per cent potassium alum by weight are added slowly with continuous agitation. This mixture is allowed to stand for twenty-four hours at room temperature and then is centrifuged. The precipitate containing the active principle from the pollen oil is washed three times with sterile normal saline solution and is diluted to a total volume of 20 milliliters.

Dilutions: The concentrated solution of the alum precipitated pyridine complex is then diluted with sterile isotonic saline solution containing 0.4 per cent phenol to the strengths convenient for testing and treatment, such as 1:5, 1:50, 1:100, and 1:500.

Cultures: Each batch of material is cultured in aerobic and anaerobic media. If aseptic technique is observed there is no difficulty in obtaining sterile extracts. In case an extract is contaminated, it may be sterilized by the use of tricresol as follows: The packed alum precipitated pyridine leaf complex is made up to the original volume of the pyridine leaf "extract" with 0.5 per cent tricresol solution and after thorough agitation is allowed to stand at room temperature for twenty-four hours. If negative cultures are obtained after this procedure the alum precipitated pyridine complex is diluted with sterile saline to the concentrations described.

4. *Tablets.*—Tablets containing the active principle of the poison ivy leaf or similar plant parts for oral treatment are made by using the various alum precipitated pyridine complexes.

In the case of poison ivy, for example, the concentrated and 1:5 concentrations of alum precipitated pyridine-ivy complex are utilized.

About 4.5 Gm. of lactose are thoroughly mixed and worked with 1 ml. of the alum precipitated pyridine-ivy "extract." This mixture is then pressed into the fifty holes of a tablet press (this amount fills this number of holes exactly). The tablets are then pressed out and allowed to dry at room temperature. Each tablet contains about 0.02 ml. of the alum precipitated pyridine-ivy "extract" used.

The alum precipitated pyridine complex settles readily on standing. Therefore, care must be taken to shake the bottle before making dilutions and before using for injections in order to obtain a homogeneous sampling.

After removal of the first supernatant fluid, all subsequent washings are colorless and after standing at room temperature for one year the alum

precipitated pyridine-ivy "extracts" have not shown any tendency to separate out into an oily fraction or to dissolve; the aqueous solution above the precipitate has remained crystal clear and colorless.

The material for patch testing consists of a blotting paper disc, one-fourth inch in diameter, which is secured to the skin with a piece of adhesive tape. Three drops of the extract to be tested are placed on each disc from a syringe equipped with a 26-gauge needle.

RESULTS

Patch tests with the alum precipitated pyridine-ivy "extract" were expected to be less active and delayed compared to patch tests obtained with the alcoholic ivy extract of the same strength due to the fact that the former was an alum precipitate and relatively insoluble in water (thus tending to be less readily absorbed by the skin) and also because it would be expected to be weaker due to the loss of small amounts of the active ivy precipitate when drawing off the saline washes.

Of twenty hypersensitive individuals showing positive poison ivy patch tests, eighteen gave the same degree of reaction with the alum precipitated pyridine-ivy "extract" and the alcoholic-ivy extract of the same approximate dilution, and only two showed a stronger test with the alcoholic-ivy extract. These results tend to show that the alum precipitated pyridine-ivy "extract" is as strong as an equivalent dilution of the alcoholic-ivy extract.

Large doses (2 to 10 ml. of the concentrated solution) of the alum precipitated pyridine-ivy "extract" were injected into guinea pigs and rabbits without any noticeable effect indicating that the material was not deleterious in doses many times that used therapeutically in human beings.

One subcutaneous injection of the alum precipitated pyridine-ivy "extract" was then administered to normal nonsensitive individuals. First each of five persons received 0.5 ml. of a 1:5,000 dilution of this "extract." One week later, after no local or systemic reactions were noted, five other individuals received 0.5 ml. of a 1:2,500 dilution. This procedure was repeated up through 0.5 ml. of the 1:50 dilution. No local reactions, soreness at the site of injection, or complaints were noted.

In phylactic and prophylactic treatment a larger initial dose of the alum precipitated pyridine-ivy complex was given than that administered when the alcoholic ivy extract was used, because this new preparation is more slowly absorbed than the alcoholic-ivy extract. Further experience with this new preparation may show that fewer but larger doses will be tolerated and give better clinical results. The following results on a small series of cases tend to substantiate this view.

Phylactic treatment in some cases began with an injection of 0.2 ml. of a 1:500 dilution, but in most cases 0.1 ml. of a 1:100 dilution of the alum precipitated pyridine-ivy "extract" was administered. This dosage in general is larger than that given when the alcoholic-ivy extract is employed, but no exacerbations, local or general, of poison ivy were noted. In almost every case

treated phylactically, relief followed the second to fifth injection. Either the same dose was repeated or small increases were made in the phylactic treatment.

Originally the plan of treatment for the prophylactic series included injections of 0.2 ml. and then 0.5 ml. of each dilution of 1:100, 1:50, and 1:5 of the alum precipitated pyridine-ivy "extract." However, several patients exhibiting a 3 plus patch test to the 1:100 dilution received an initial injection of 0.1 ml. of 1:100 dilution with no exacerbation of poison ivy, and completion of prophylactic treatment resulted in a good season with no poison ivy dermatitis or only a mild rash whereas, in the previous year, with the alcoholic ivy treatment there had been severe poison ivy dermatitis. Sensitive patients giving a negative or 1 plus reaction to 1:100 dilution were usually given an initial injection of 0.1 ml. of a 1:20 or 1:50 dilution of the alum precipitated pyridine-ivy "extract" with no poison ivy exacerbations, and again, after five injections of increasing doses, they experienced a season free of poison ivy rash.

The following treatment schedule was generally used: 0.1 ml. of 1:50 dilution; 0.4 ml. of 1:50 dilution; 0.8 ml. of 1:50 dilution; 0.2 ml. of 1:5 dilution; 0.5 ml. of 1:5 dilution.

In 1943, twelve sensitive persons were treated who continued to have poison ivy dermatitis after injections of the alcoholic-ivy extract. In 1944, these twelve patients were treated with the alum precipitated pyridine-ivy "extract," and six reported no poison ivy dermatitis during the season although in the same surroundings as in 1943; five had much less poison ivy dermatitis than during the previous year, usually consisting of one mild attack; and only one experienced no improvement.

There were sixteen sensitive persons treated in a similar manner in 1945 with the alum precipitated pyridine-ivy complex and excellent clinical results were obtained. In only one case did a severe outbreak occur and the lesions appeared on skin areas in actual contact with the poison ivy plant.

Guinea pigs were given a single intraperitoneal injection of 2 ml. of the concentrated alum precipitated pyridine-ivy "extract" and care was taken so that none of the ivy complex came in contact with the skin. Twenty days later, the guinea pigs were patch tested on the back as described for human beings except that an area of their skin was first depilated with Neet or Imra (commercial depilatories) and thoroughly rinsed and 3 drops of the concentrated alcoholic-ivy or concentrated alum precipitated pyridine-ivy were placed on the blotting paper disc. The patches were secured with adhesive and rolled bandage and remained on the skin for twenty-four hours. The sites were usually negative when the patches were removed. However, forty-eight to seventy-two hours later, erythema of varying degrees, with and without vesiculation, appeared. In most animals showing a positive reaction, the onset of the rash was gradual, reaching maximum intensity sometimes four to six days after the patch was removed, and resembling somewhat the gradual increase in severity of reactions seen in some sensitive human beings after contact with the plant.

Two guinea pigs developed a generalized poison ivy rash over their entire bodies seventeen days after receiving 2 ml. of the concentrated alum precipitated pyridine-ivy "extract" intraperitoneally. The rash was characterized by

small vesicles and erythema over the entire body. On the flanks and sides of the animal, the skin was bloody and sore at some points tending to indicate that they had scratched themselves there against the cages. The hair had become so thin that the skin could be seen readily.

Twelve normal guinea pigs when patch tested in an identical manner generally gave negative results. Two of these pigs gave a positive reaction under the patch consisting of erythema when the patch was removed. The reaction did not increase in intensity, and no vesiculation occurred.

Many workers have attempted to produce poison ivy sensitization by the parenteral route without success. Landsteiner and Chase[18] concluded from their experiments on sensitization of the skin to simple chemicals, that the lymphatics are of considerable importance in the spread of cutaneous sensitivity.

With this alum precipitated pyridine-ivy principle it has been possible, for the first time, we believe, to sensitize a guinea pig by parenteral injection of a poison ivy "extract." If this means that this aqueous suspension of the ivy principle is in an antigenic form more readily available to the animal for sensitization, it may also prove to be more useful as an antigen in human beings for desensitization. There is also the fact that it is an active ivy principle suspended in aqueous solution, which makes it much easier to administer than the alcoholic or oily ivy extracts.

A total of 125 poison ivy sensitive individuals were treated by Dr. A. Harvey Neidorff, Altoona, Pa.,[19] in 1944. Twenty-five of these cases received the prophylactic treatment as previously described with the alum precipitated pyridine-ivy complex suspended in aqueous solution; twenty-three of these patients had a successful season; two had flare-ups of poison ivy dermatitis which were relieved by subsequent injections of this ivy complex. There were one hundred individuals who had acute poison ivy dermatitis; fifty of these were treated with the alum precipitated pyridine-ivy "extract" (62 per cent obtained relief after the fourth injection and 94 per cent obtained relief after the sixth injection) 25 persons were treated with the oily ivy extract (60 per cent obtained relief after the fourth injection) and 25 persons were treated with the alcoholic ivy extract (64 per cent obtained relief after the sixth injection).

SUMMARY

1. A method is presented for the preparation of a new product from poison ivy, poison oak, poison sumac, primrose, and the like and pollen oils, whereby the active principle is suspended in aqueous solution.

2. The new product suspended in aqueous solution is shown to be nontoxic and nonirritating.

3. The alum precipitated pyridine-ivy complex suspended in saline solution is as active as an equivalent dilution of the alcoholic ivy extract.

4. Sensitive patients treated phylactically with the alum precipitated pyridine-ivy "extract" were relieved by the second to fifth injection.

5. A group of twelve patients treated prophylactically in 1943 with the alcoholic extract with poor results were treated in 1944 with the alum precipi-

tated pyridine-ivy "extract" with good clinical results. Sixteen other sensitive individuals experienced a season practically free from poison ivy dermatitis following injections of a precipitated pyridine-ivy "extract."

6. Guinea pigs were sensitized by one intraperitoneal injection of the alum precipitated pyridine-ivy "extract" as shown by positive patch tests (twenty-one days after the sensitizing injection) to 3 drops of the concentrated alum precipitated pyridine-ivy "extract" or alcoholic-ivy extract.

REFERENCES

1. Pfaff, F.: On the Active Principle of Rhus Toxicodendron and Rhus Venenata, J. Exper. Med. **2**: 181, 1897.
2. Acree, S. W., and Syne, W. A.: Some Constituents of the Poison Ivy Plant, Am. Chem. J. **36**: 301, 1906; On the Composition of Toxicodendrol, J. Biol. Chem. **2**: 547, 1906.
3. McNair, J. B.: The Poisonous Principle of Poison Oak, J. Am. Chem. Soc. **38**: 1417, 1916; Lobinol—A Dermatitant From Rhus Diversiloba, ibid. **43**: 159, 1921.
4. Majima, R.: Chief Constituent of Japanese Lac. VIII. Position of the Double Bonds in the Side Chain of Urushiol and Proof That Urushiol Is a Mixture, Ber. **55**: B: 172, 1922.
5. Hill, G. A., Mattacotti, V., and Graham, N. D.: The Toxic Principle of the Poison Ivy, J. Am. Chem. Soc. **56**: 2736, 1934.
6. Mason, H. S., and Schwartz, L.: The Toxic Principles of Poison Ivy, J. Am. Chem. Soc. **64**: 3058, 1942.
7. Landsteiner, K., and Jacobs, J.: Studies on Sensitization of Animals With Simple Chemical Compounds, J. Exper. Med. **64**: 625, 1936.
8. Keil, H.: Value of the Patch Test in Poison Ivy, Dermatitis, J. ALLERGY **15**: 259, 1944.
9. Spain, W. C., and Cooke, R. A.: Dermatitis Venenata: Observations Upon the Use of a Modified Extract From Toxicodendron Radicans, J. Immunol. **13**: 93, 1927.
10. Clock, R. O.: Rhus Dermatitis: Its Treatment With Poison Ivy Extract, M. J. & Record **122**: 93, 1925.
11. Caulfield, A. H. W.: Prevention of Poison Ivy Dermatitis by the Intramuscular Injection of "Rholigen," Canad. M. A. J. **37**: 18, 1937.
12. Vaughan, W. T.: Practice of Allergy, St. Louis, 1939, The C. V. Mosby Co.
13. Shelmire, B.: Contact Dermatitis From Weeds: Patch Testing With Their Oleoresins, J. A. M. A. **113**: 1085, 1939.
14. Shelmire, B.: The Poison Ivy Plant and Its Oleoresin, J. Invest. Dermat. **4**: 337, 1941.
15. Sollman, T.: A Manual of Pharmacology, ed. 6, Philadelphia, 1942, W. B. Saunders Co.
16. The Merck Index, ed. 5, Merck & Co., Inc., Rahway, N. J. 1940.
17. Stull, A., Cooke, R. A., and Chobot, R.: The Allergenically Active Substance in Ragweed Pollen. A Chemical and Biological Study, J. Biol. Chem. **92**: 569, 1931.
18. Landsteiner, K., and Chase, M. N.: Studies on the Sensitization of Animals With Simple Chemical Substances. VI. Studies on the Sensitization of Guinea Pigs to Poison Ivy, J. Exper. Med. **69**: 767, 1939.
19. Personal communication.

Original Articles

A STUDY OF THE INHERITANCE OF RESPIRATORY ALLERGIES

KARL A. STILES, M.S., PH.D.,* AND ELIZABETH J. JOHNSTON, A.B.,
EAST LANSING, MICH.

INTRODUCTION

IT IS now quite generally agreed that heredity plays an important role in the etiology of some allergies. As early as 1650 a familial incidence of asthma was reported. The first serious modern study of the heredity of asthma and hay fever was undertaken by Cooke and Vander Veer[13] in 1916. They concluded that the mode of inheritance was simple Mendelian dominance. Adkinson,[1] in 1920, favored the idea of a simple recessive characteristic. In 1924, Spain and Cooke[25] said it was possibly a single dominant gene, or perhaps dominant and multiple, the component parts being separately inherited. They claimed the latter hypothesis might explain the individual variation in the degrees of hypersensitiveness as well as the variation in the age of onset.

Clarke, Donnally, and Coca,[11] in 1928, showed that there is a tendency for the children of asthmatic parents to develop asthma and for those of hay fever parents to develop hay fever. They submitted evidence in support of the conclusion that the bronchial and upper respiratory tract shock tissues are subject to separate hereditary influence. However, it is not a rule that the progeny must always develop the same allergic manifestation as their parents did.

Bell and Eriksson,[5] in 1931, made studies on the transmission of the hypersensitiveness from mother to child through the placenta. This gave rise to subsequent studies on placental or serum sensitization. Ratner,[21] in 1932, said that "congenital protein hypersensitiveness" was clearly established. In 1934, Bray[7] said that active sensitization in utero was possible in man, but that passive sensitization was, in all probability, rare. He also thought, and Rowe[22] agreed with him, in 1937, that more statistics were necessary before a correct inference could be made as to whether allergy was a dominant or a recessive trait.

The same year (1934) Bucher and Keeler[10] reported allergy transmission as a dominant gene in five generations of 454 individuals. Wiener, Zieve, and Fries, in 1936,[28] presented a recessive theory but with explanations for the irregularities.

An attempt to discover the exact mode of the inheritance of atopy is extremely difficult because there are so many unknown factors. Further intensive collection of data and study are needed to solve this problem. In view of this

Contribution from the Science Laboratories of Coe College No. 21, N.S.
Aided by an academy grant from the American Association for the Advancement of Science through the Iowa Academy of Science.
*From Michigan State College, East Lansing, Michigan.

need, it seems worth while to present a family of five generations showing familial atopy.

NOTES ON THE PEDIGREE

This family of five generations (Fig. 1) has been studied in regard to the inheritance of respiratory allergies: namely, asthma, hay fever, and bronchial troubles. This is a comparatively large family, I-1 having had nine children, 63 grandchildren, and 160 great-grandchildren. Some form of respiratory disease has appeared in every branch of the family.

I-1 was a Scottish immigrant who came to Canada about 1850. He had a very severe case of asthma and for periods of six weeks was unable to lie down. He suffered all his life.

The nine branches of family, that is, the descendants of each of the nine children of I-1, will be described separately.

II-1, the eldest daughter, developed bronchitis after a severe cold at about the age of 75 years. In adult life, III-15, an offspring of II-1, had asthma of low expressivity in the winter. All of the fourth and fifth generations have appeared normal. This branch of the family has always lived north of Toronto, Canada, so the weather conditions may be a contributing factor to this low percentage of incidence, as will be shown later.

II-3, a normal person, had nine children, two of whom suffered with asthma. III-26 had a very severe case. One of his four children, IV-45, suffers from bronchitis, and the daughter, V-11, in turn, has hay fever. III-28, also, had an acute case of asthma and hay fever. A change of climate to Duluth, Minnesota, was thought to have helped; the attacks became lighter as he became older. Both of his children, IV-47 and IV-49, suffered from hay fever. IV-49 had his first attack at the age of about 38, and V-12, his son, also suffers from hay fever. III-34, a normal offspring, had five children, one of whom, IV-72, suffered from hay fever, while another, IV-73, suffered from asthma. A change of climate helped in the latter case. III-36, a normal offspring, had nine children, one of whom, IV-85, had fever. V-32, one of the five children of IV-85, also has hay fever. V-46, a grandchild of III-38, now 10 years old, has suffered from hay fever since the age of 3. In this case, three generations were skipped.

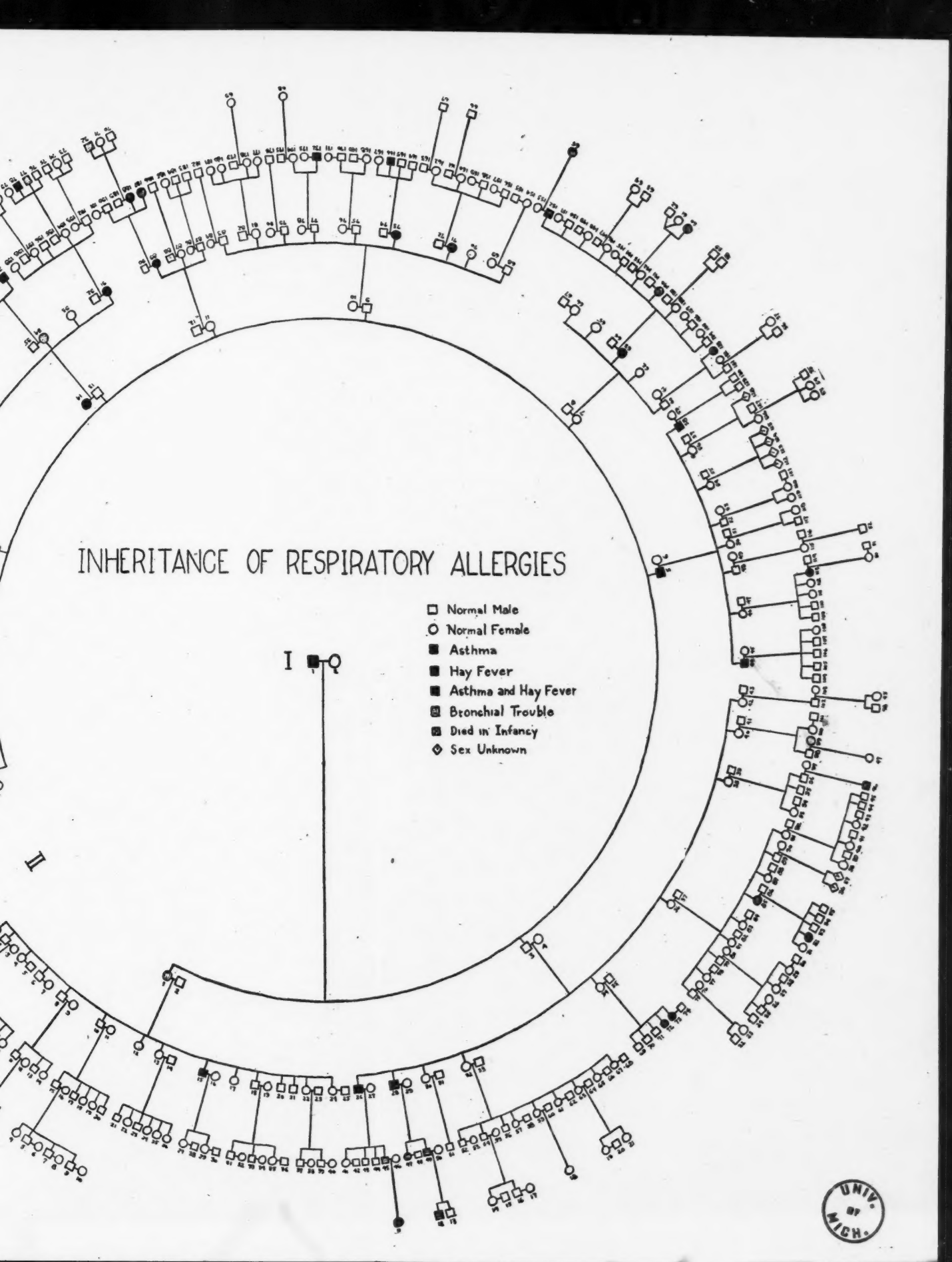
II-5 had a severe case of asthma, which was relieved when he lived in the mountains of Washington. He had eight children, two of whom, III-44 and III-58, developed asthma which was worse in winter than in summer. All the children of these two sufferers appear normal, but III-46, an unaffected sister, had five children, one of whom, IV-113, has asthma.

II-7, a normal individual, had five children, one of whom, III-63, had an acute case of hay fever and asthma. Her first attack was at the age of 33, and she suffered until her death at the age of 59. Two of her ten children have hay fever. IV-140 showed symptoms of hay fever at the age of 36, and she has it

---

Fig. 1.—Inheritance of respiratory allergies. A pedigree chart showing the inheritance of respiratory allergies. The incidence in this family of five generations is 22.4 per cent as opposed to the incidence in the general population of approximately 7 per cent. The appearance of this trait in families of normal parentage as well as those of affected parentage seems to indicate irregular dominance as the mode of inheritance.

I
II
III
IV
V


INHERITANCE OF RESPIRATORY ALLERGIES
Normal Male
Normal Female
Asthma
Hay Fever
Asthma and Hay Fever
Bronchial Trouble
Died in Infancy
Sex Unknown
I
II

UNIV. OF MICH.

every fall in a mild form, with the exception of the two years she lived in California when she showed no symptoms. IV-152 has had severe asthma and hay fever since the age of 18, and every fall goes north to Canada for relief. V-65, daughter of IV-152, had hay fever for the first time last year, when she was 3 years old. V-60, who is 12 years old at this writing, is the daughter of IV-142 (unaffected); she has had hay fever in a mild form every fall for about five years. III-60, a normal person, had two children, one of whom, IV-133, has had hay fever for about twenty years, showing the first symptoms at the age of 10.

II-9, an unaffected son, married a normal woman and had nine children, two of whom, III-71, and III-73, developed asthma and hay fever severely during adolescence. No offspring of III-71 developed asthma, but one of the four children of III-73, IV-166, has acute hay fever and asthma all year long. III-77, an unaffected son of II-9, had two children, one of whom, IV-172, suffered violently with asthma as a child. He has improved since becoming an adult, but still has slight attacks in winter. In this case, the trait skipped two generations.

II-11, a normal individual, had three children, one of whom, III-89, had asthma in her childhood until about the age of 12 years. At that time she had the measles and has never been troubled with asthma since. One of her daughters, IV-188, has had two attacks of asthma, one at the age of 35 years, just preceding the birth of her first child, and another at the age of 49 years. She has had hay fever for the last few years. When she was 8 years old, she had severe pneumonia and has always been subject to many colds. The youngest of her three children, V-72, has been subject to bronchial trouble. IV-187, another daughter of III-89, had hay fever for a few years, starting at the age of 20. She was treated for temporary relief and has not suffered since, although that was twenty-five years ago. This branch of the family has always lived in Texas.

The next branch of the family is very interesting. The son, II-13, appeared normal, and he married a woman, II-14, with asthma, more extreme in winter than in summer, and a great deal of asthma appears in their offspring. Of their four children, three were affected. III-91 had no trouble as a child, but asthma developed while she was in college and became steadily worse through the years. This was also the course it took in III-96, beginning when she was about 30 years of age. III-94 had bronchial trouble as a child but has not suffered in adult life. By contrast, the fourth child, III-93, was amazingly free from colds and had no symptoms of asthma. None of III-91's five children has yet shown signs of it, but V-78, a son of IV-194, has an extreme case of asthma, just like his grandmother's. Another, V-77, has trouble with bronchial coughs. Both V-78 and V-77 are under 10 years of age. One of III-94's three offspring, IV-200, has a tendency toward asthma, with many colds affecting his lungs. Neither of IV-200's two children shows it, but his normal sister, IV-202, has two children, one of whom, V-85, suffers from bronchial trouble in the winter, but is free from it in summer.

At this point it will be noted that III-96 married a normal man, III-97, whose mother was an asthma sufferer. The ancestry of III-97 was not included in the pedigree chart in order to avoid confusion, since the chart is of just one family, the descendants of I-1. Three of the four children of III-96 and III-97 show asthmatic tendencies. This is the same proportion as in the offspring of normal II-13, with an asthmatic father, and II-14, who had asthma. Of these three offspring, one, IV-207, now thirty years of age, suffered as a child, but not in adulthood, while the other two, IV-209 and IV-211, have suffered in the winters since adolescence. IV-211 had her first attack at the age of 9, following a long illness from scarlet fever. V-88, 4 years old at this writing, one of the two children of IV-207, has frequent colds and slight bronchial trouble.

The eighth offspring of I-1, who is II-15, had an extreme case of asthma, being afflicted all year long. Of his four children, three were affected. III-103 was a very bad case, just like his father. Of III-103's six children, only one, IV-226, developed asthma, and his three children are all normal. III-98 showed symptoms in young womanhood and is gradually becoming worse. Her two children are both normal. III-100 suffers with bronchial coughs.

II-17 had asthma, especially in cold weather. Of his six children, one, III-109, was affected with both asthma and hay fever in her twenties. When she went to Colorado, she obtained some relief, but she died at the age of 33 and was getting worse at the time of her death. All of her five children were normal, but the 23-year-old son, IV-249, of her normal brother, III-113, has had hay fever since the age of 10, except during the last two years while he has been serving in the Navy in the South Pacific Area.

Thus we see that of the nine children of this affected man, I-1, four are affected; of 63 grandchildren, 16 are affected; and of 160 great-grandchildren, 20 are affected. This gives a ratio of approximately one affected to five unaffected.

DISCUSSION

Studies of the inheritance of human allergic diseases are not likely to give data that are in perfect agreement with Mendelian ratios. For, in the first place, it is difficult to tell whether the manifestation was brought about by definite germinal transmission or as a result of sensitization while in utero. Second, it is impossible to control the material; matings occur as one finds them, not as one wishes. Third, generations are long and families not large enough to be sure that all possible combinations of genes are present. Fourth, individuals possessing the predisposition may not manifest it at all or may have manifested it in a form not recognized or remembered, while in children the hereditary factor may exist, but not show as a clinical state until later in life. Finally, the extreme multiplicity of types and causes and the same type arising from different causes is a difficulty. All these factors add to the confusion in studies of atopy.

Physiology.—It is generally agreed that it is not the specific sensitization that is inherited but rather the predisposition to develop allergic reactions. Cooke and Vander Veer[14] were the first to support this principle.

When the shock tissues, in this case the respiratory tissues, come in contact with the atopen (the critical substance to which the shock tissues are sensitized), a specific antibody is formed in the body cells. The presence of the antibody makes the tissues of the individual permanently hypersensitive to the atopen when introduced. There are many atopens, both protein and nonprotein, which produce the asthma and hay fever. Pollen and food are the most common protein atopens producing asthma and hay fever attacks.

In the pedigree under study, the weather seems to have an effect as an environmental factor. The symptoms did not appear as frequently among those who lived in the cooler northern regions. III-28 and IV-152 went north for relief, and II-5 and III-109 found relief in the mountains. Yet the majority of all 53 cases seem to be more severe in the winter than in the summer; I-1 had to give up farming in the winters, IV-140 showed no symptoms while living in the warm climate of California, and IV-249 has not been affected since he went to the South Pacific Area. IV-73 and IV-113 claim to have found relief in a change of climate. Mohr[16] and Preuner[19] both say that wind direction and sharp air movements bring on attacks. Rowe[23] says that hypersensitive individuals frequently lose their symptoms in the summer or by going inland 5 or 10 miles. The variations in climatic results may be due to the fact that the specific atopen to which the particular individual is allergic is not present in cooler regions, or, as the case may be, warmer regions.

Pressburger[18] believes asthmatic attacks are precipitated by an acute state of dehydration of large areas of lung tissue. Only oxygen dissolved in moisture is absorbed across the alveolar membrane. When, by reason of allergy, the bronchial glands suddenly cease to produce a moist coating for the alveolar membrane, oxygen can no longer be absorbed from the affected area, and an asthmatic attack results.

It is true that two individuals do not react to the same atopen in the same way. One may suffer from hay fever alone, the other only from bronchial asthma.

Degree of Inheritance.—The incidence of hay fever and asthma in the general population is approximately 7 per cent, but in the family here reported it is 22.4 per cent. The high incidence of allergy in this family suggests strongly that an hereditary factor is involved in the etiology of the disease.

There are no cases of bilateral family history, that is, both parents affected. Of the 51 cases where the history is known, 64.7 per cent are unilateral (one parent affected), while 35.3 per cent are negative (neither parent having symptoms). Table I is a summary according to unilateral or negative inheritance.

The familial nature of the allergic tendency is clearly demonstrated in this group: the more direct the inheritance, the larger the percentage of offspring affected.

TABLE I

	TOTAL OFFSPRING	ALLERGIC	PER CENT
Unilateral	134	33	24.5
Negative	189	18	9.5

TABLE II

	BEFORE 10 YEARS OF AGE	ADOLESCENCE	AFTER 20 YEARS OF AGE
Unilateral	18.2%	24.3%	57.5%
Negative	33.3%	38.9%	27.8%

Age Incidence.—Spain and Cooke,[26] Cooke and Vander Veer,[15] Balyeat,[3] Rackemann,[20] Peshkin,[17] Bray,[9] and Coca[12] agree that the degree of inheritance determines the age of onset. In the bilaterally affected group, the largest percentage is affected in the first decade, while the larger percentage of the unilaterally or negatively affected group does not show the symptoms until a later age. However, the more complete the familial factor, the earlier the onset. Table II shows the age of onset in the family being reported according to the degree of evident inheritance.

We see here that the largest percentage in the unilateral group was not affected until adulthood, while the largest percentage in the negative group showed symptoms during adolescence. However, the percentage affected was more nearly equal during each of the three periods in the negative group. There may be several explanations for the earlier age of onset in this negative group: (1) modifying and interacting genes to produce hypersensitivity earlier, (2) especially strong contact with the sensitizing atopen, (3) sensitization in utero which manifests itself early, and (4) inadequate number of cases.

Sex Incidence.—Bray[8] found that twice as many males as females were affected before puberty, after which clinical symptoms of atopy appeared more often in females. Therefore, he concluded that puberty must be a definite milestone, after which a great number of males improve and a greater number of females develop symptoms. He thought that puberty must exert some beneficial effect upon the symptoms in the male and some deleterious effect upon the female. He concluded that over twice as many males as females are likely to be affected before puberty; the probability of recovery at puberty is much greater in the boy than in the girl; and the chance of developing allergic manifestations after that age is greater in the female than in the male. Table III shows how these conclusions apply in this family.

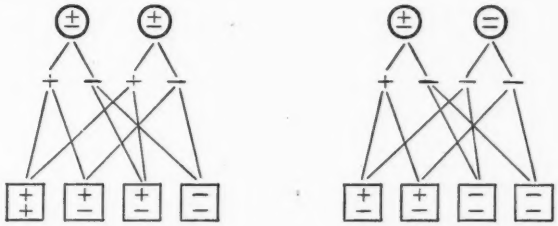
TABLE III

	BEFORE PUBERTY	AFTER PUBERTY
Males	75% (18 cases)	25% (6 cases)
Females	27.6% (8 cases)	72.4% (21 cases)

Of the 53 cases of atopy in this pedigree, 24 are male and 29 are female. So there is no basis here for an argument that atopy favors one sex or the other. However, it does appear that more males are affected before puberty and more females are affected after puberty. In three of the 18 male cases which developed before puberty, the symptoms disappeared for the most part during adolescence.

Modes of Inheritance.—Cooke and Vander Veer[13] considered atopy to be transmitted from parent to child as a dominant Mendelian character. Their genetical analysis is as follows.

Atopy is dependent upon a single pair of genes. It is often impossible in human genetical studies to determine whether an individual is homozygous or heterozygous. If the sensitization trait is pure, or homozygous, in one parent, *all* the offspring should be sensitized whether the trait in the other parent is pure or mixed. But there has been no family studied large enough and with all children sensitized to be sure that this is the case. Assuming then that all parents, although apparently sensitized, are heterozygous with respect to the sensitization trait, there should be, according to the Mendelian laws, 75 per cent of the offspring sensitive in the case of bilateral inheritance and 50 per cent of the offspring sensitive in unilateral inheritance. The following chart illustrates these theoretical facts:



75% Dominant 50% Dominant

The figures of 67.5 per cent and 60 per cent obtained in the survey of Cooke and Vander Veer[13] were thought by them to approximate roughly the theoretical 75 and 50 per cent. With regard to the cases of negative family histories they blame the limitations of their methods of ascertaining the family histories. However, the 24.5 per cent of the unilateral cases in the pedigree being discussed does not approximate the theoretical 50 per cent very closely. It is possible, though, that more cases may develop as the ages of some of the individuals increase. This theory of Mendelian dominance has been favored by Spain and Cooke,[25] Bucher and Keeler,[10] Balyeat,[4] Bray,[6] Smith,[24] and Alexander.[2]

In 1936, Wiener, Zieve, and Fries[28] rejected the dominant theory since it failed to explain why, in more than one-half of the pedigrees, both parents are normal. They rejected the recessive theory presented by Adkinson in 1920 since there are pedigrees in which both parents are affected and some of the children are normal. They presented a theory which inclines toward recessiveness, but explains why two allergic parents may have apparently normal children.

According to Wiener, Zieve, and Fries,[28] the inheritance of the allergy may depend upon a single pair of allelic genes; N, the normal or nonallergic gene which tends to be dominant; and A, the allergic gene tending to be recessive. A person with two allergic genes will develop frank symptoms of allergy; a person with two normal genes will never develop allergy; while a person with

mixed genes is a potential allergy patient and either will develop symptoms later in life or will go through life without symptoms, but will still transmit the gene to the next offspring.

Wiener, Zieve, and Fries state that puberty is the deciding point; that a person homozygous for atopy will manifest it before puberty, while a heterozygous individual will develop it after puberty, or not at all. This could be modified to say that a person with mixed genes could develop hay fever or asthma any time during life, the determining factor being not only puberty, but also some environmental factor such as the weather, presence of the critical atopen, sex, or the time that the gene comes to expression.

The following figure shows the various possible combinations of mating:

	a	*b*	*c*
Parent 1	N-N	N-N	N-A
Parent 2	N-N	N-A	N-A
	NN NN NN NN	NN NN NA NA	NN NA NA AA
	100%N	50%N 50%NA	25%N 50%NA 25%A

	d	*e*	*f*
Parent 1	N-N	N-A	A-A
Parent 2	A-A	A-A	A-A
	NA NA NA NA	NA NA AA AA	AA AA AA AA
	100%NA	50%NA 50%A	100%A

It must be remembered that an N-A parent may be normal or may be allergic, especially later in life. With this in mind, there are several possible results of mating.

Both parents normal (represented by *a*, *b*, and *c*): Twenty-five per cent of the offspring in *c* will be definitely allergic. Fifty per cent of those in *b* and *c* will be potentially allergic and may or may not manifest symptoms. Of 12 possible matings of normal parents (*a*, *b*, *c*), one will be definitely allergic; four, or one-third, will be potentially so; and seven will inherit no allergy.

One parent allergic; one normal (represented by *b*, *c*, *d*, and *e*): Assuming that the second parent in *c* (who is potentially allergic) has manifested symptoms, in *b*, as we have seen, 50 per cent will be potentially allergic; 100 per cent will be potentially allergic in *d*; and 50 per cent will be potentially allergic in *e*, while the other 50 per cent in *e* will be definitely so. In *c*, 25 per cent will be definitely allergic, and 50 per cent will be potentially so.

Both parents allergic (represented by *c*, *e*, and *f*): Wiener, Zieve, and Fries compute that one-fifth to one-sixth of the potential allergics (N-A genotype) will develop symptoms. The remaining 80 to 85 per cent will go through life without the allergy, but will transmit the gene to their offspring. Whether or not the allergy will appear in their offspring depends upon the gene of the mate.

The Wiener-Zieve-Fries explanation for inheritance of atopy agrees more closely with the pedigree presented here than does the Cooke-Vander Veer simple dominance hypothesis. In two cases (II-13 and III-97) an apparently

normal person who may have been potentially allergic married an individual in whom the symptoms appeared, and 75 per cent of the offspring in both cases manifested the allergy. Of course, the families are too small for the ratios to be statistically reliable, but it is interesting to note that more allergy appeared when there was atopy on both sides of the family.

The Wiener-Zieve-Fries genetical analysis of the inheritance of atopy has something in common with an irregular dominance interpretation in that the trait might always come to expression in the homozygote but appearing irregularly in the heterozygote. The difference is that, in irregular dominance, the gene for the character is considered a dominant one, while according to the Wiener-Zieve-Fries theory it is considered recessive. The data presented by the authors can just as well be explained by the theory of irregular dominance with low penetrance of the gene for respiratory allergies in the heterozygous condition, as by Wiener, Zieve, and Fries' theory of recessiveness. The same arguments are supported by either theory. There does not seem to be anything explained by this theory of recessiveness that could not be explained by irregular dominance; therefore, on the basis of our data, we interpret respiratory allergies to be an irregular dominant trait. The low penetrance of the gene and variable expression may be due to either environmental or genetic modifiers, or a combination of both genetical and environmental influences.

SUMMARY

1. A family of five generations with 232 persons was studied with respect to the inheritance of respiratory allergies. The incidence in the family studied was 22.4 per cent in contrast with approximately 7 per cent in the general population.

2. In studying the inheritance of atopy, perfect Mendelian ratios are not likely to be obtained, due to the complexity of both environmental and hereditary factors involved.

3. The specific sensitivity does not appear to be inherited, but rather the capacity, or the predisposition, to become hypersensitive.

4. The manifestations of the symptoms are influenced by many factors and their interactions, including presence of the atopen, climate, degree of inheritance, age, and sex.

5. Our data suggest that respiratory allergy may be interpreted as an irregular dominant character. The gene exhibits low penetrance with variable expressivity.

REFERENCES

1. Adkinson, June: The Behavior of Bronchial Asthma as an Inherited Character, Genetics 5: 363, 1920.
2. Alexander, H. L.: Synopsis of Allergy, St. Louis, 1941, The C. V. Mosby Co., p. 21.
3. Balyeat, R. M.: The Hereditary Factor in Allergic Diseases, Am. J. M. Sc. 176: 332, 1928.
4. Balyeat, R. M.: The Hereditary Factor in Allergic Diseases, Am. J. M. Sc. 176: 336, 1928.
5. Bell, S. D., and Eriksson, Z.: Studies in the Transmission of Sensitization From Mother to Child in Human Beings, J. Immunol. 20: 447, 1931.
6. Bray, G. W.: The Hereditary Factor in Asthma and Other Allergies, Brit. M. J. 1: 386, 1930.

7. Bray, G. W.: Hereditary Factor in Hypersensitiveness, Anaphylaxis, and Allergy, J. ALLERGY 2: 205, 1931.
8. Bray, G. W.: Hereditary Factor in Hypersensitiveness, Anaphylaxis, and Allergy, J. ALLERGY 2: 211, 1931.
9. Bray, G. W.: Recent Advances in Allergy, Philadelphia, 1931, P. Blakiston's Son & Co., p. 79.
10. Bucher, C. S., and Keeler, C. E.: The Inheritance of Allergy, J. ALLERGY 5: 611, 1934.
11. Clarke, J. A., Jr., Donnally, H. H., and Coca, A. F.: Studies in Specific Hypersensitiveness: On the Influence of Heredity in Atopy, J. Immunol. 15: 9, 1928.
12. Coca, A. F.: Studies in Hypersensitiveness: On the Influence of Heredity in Atopy, J. Lab. Clin. Med. 12: 1135, 1927.
13. Cooke, R. A., and Vander Veer, A., Jr.: Human Sensitization, J. Immunol 1: 201, 1916.
14. Cooke, R. A., and Vander Veer, A., Jr.: Human Sensitization, J. Immunol. 1: 211, 1916.
15. Cooke, R. A., and Vander Veer, A., Jr.: Human Sensitization, J. Immunol. 1: 207, 1916.
16. Mohr, G.: Weiterer Beitrag zur Frage des Zusammenhanges zwischen Asthmaanfall und Wetter, Balneologe 6: 75, 1939.
17. Peshkin, M. M.: Asthma in Children, Am. J. Dis. Child. 36: 95, 1928.
18. Pressburger, R.: Die Dehydrationstheorie desechten bronchialasthmatischen Anfalles, Schweiz. med. Wchnschr. 71: 581, 1941.
19. Preuner, R.: Allergiestudien. II. Die Beziehungen zwischen experimentellem Asthma bronchiale und Witterung, Ztschr. f. Hyg. u. Infektionskr. 122: 320, 1939.
20. Rackemann, F. M.: Clinical Allergy: Asthma and Hay Fever, New York, 1931, The Macmillan Co., p. 138.
21. Ratner, B.: Placental Transmission of Alimentary Anaphylaxis, Proc. Soc. Exper. Biol. & Med. 30: 88, 1932.
22. Rowe, A. H.: Clinical Allergy, Philadelphia, 1937, Lea & Febiger, p. 44.
23. Rowe, A. H.: Seasonal and Geographic Influences on Food Allergy, J. ALLERGY 13: 55, 1941.
24. Smith, A. E.: A Report of the Occurrence of Hypersensitiveness in Five Generations of One Family, J. Missouri M. A. 24: 382, 1927.
25. Spain, W. C., and Cooke, R. A.: Studies in Specific Hypersensitiveness: Familial Occurrence of Hay Fever and Bronchial Asthma, J. Immunol. 9: 534, 1924.
26. Spain, W. C., and Cooke, R. A.: Studies in Specific Hypersensitiveness: Familial Occurrence of Hay Fever and Bronchial Asthma, J. Immunol. 9: 524, 1924.
27. Vaughan, W. T.: Practice of Allergy, St. Louis, 1939, The C. V. Mosby Co., p. 74.
28. Wiener, A. S., Zieve, I., and Fries, J. H.: The Inheritance of Allergic Disease, Ann. Eugenics 7: 141, 1936.

AN ALLERGIC REACTION FOLLOWING TYPHUS-FEVER VACCINE AND YELLOW-FEVER VACCINE DUE TO EGG YOLK SENSITIVITY

MAJOR SIMON S. RUBIN,* M.C., ARMY OF THE UNITED STATES

WITH the increased use of virus and rickettsial vaccines prepared from infected chick embryo and chick egg yolk sac, we can expect to see various allergic manifestations due to egg and chicken sensitivity.

Swartz[1] reported a systemic allergic reaction induced by yellow-fever vaccine in an allergic individual who was sensitive to egg white and chicken meat. Sulzberger and Asher[2] reported three cases of urticaria and erythema multiforme-like eruptions appearing thirty-six or more hours after yellow-fever vaccine inoculations. Accompanying the skin manifestations were general malaise, joint pains, headache, fever, pruritus, nausea, and vomiting. According to Sulzberger, the clinical picture, the incubation period, and the course of the manifestations suggest a sensitization or an allergic mechanism identical with mild serum sickness, rather than an infectious or direct virus effect.

Berge and Hargett[3] have produced anaphylaxis in guinea pigs following sensitization with chick-embryo yellow-fever vaccine and normal chick embryo. They also showed that, when doses of comparable nitrogen content are employed, chick-embryo extract from ten-day (or younger) embryos is found to be weakly anaphylactogenic, while that from fourteen-day embryos is highly so.

This report is that of a soldier who developed angioneurotic edema, blocking of the nose, and tightness in the chest shortly after receiving typhus-fever and yellow-fever vaccines. The interesting finding in this case is that an allergic individual gives a history of egg yolk sensitivity which was definitely corroborated by various tests, as will be shown later.

From the available literature, there is not a similar report of a case in which the individual was only sensitive to egg yolk and not also sensitive to egg white. Tuft[4] states that, of the various parts of the egg, sensitization is most usual to egg white or its component parts; however, sensitization to egg yolk has been reported, but its actual existence is doubtful. Walzer[5] states that it is doubtful that sensitivity to egg yolk occurs independently of allergy to egg white. In Feinberg's[6] book, he reports: "The egg white is the main source of the egg allergy. Although we do not deny the possibility of allergy to the yolk, we have never seen an authentic case nor do we know of one reported. We have never seen an instance in which egg yolk preparations caused a reaction better than (or equal to) egg white."

*On leave from Northwestern University Medical School Allergy Department.

CASE REPORT

A 19-year-old soldier was admitted to the hospital with a diagnosis of angioneurotic edema. His chief complaints were painless swelling of the eyelids, bridge of nose, and both cheeks, blocking of the nose, and pain in the chest. These symptoms came on about one and one-half hours after receiving inoculations of typhus-fever and yellow-fever vaccines. The pain in the chest lasted about five minutes and was not aggravated by deep breathing. The swelling of the face persisted for two days.

The past history of this patient is very significant. He has had spring and fall hay fever for eight years; however, there is no history of asthma. He has been sensitive to eggs since childhood and has not eaten whole eggs since infancy because they caused him to vomit. He can eat the white of a hard-boiled egg without any trouble.

His family history is essentially negative except that his father has hay fever.

Physical examination was essentially negative except for the angioneurotic swelling of eyelids, bridge of nose, and both cheeks. There were no physical findings in the cardiac and respiratory systems to account for the pain in his chest. The blood pressure was 120/80.

Cutaneous testing revealed the following reactions: chicken feathers, 0; chicken meat, 0; egg yolk, ++++; and egg white, 0.

Intracutaneous testing with freshly prepared antigens from egg gave the following reactions: egg white 1:1,000, ±; egg white 1:10, ±; and egg yolk 1:1,000, ++++.

Results of retesting at a later date are recorded in Table I.

TABLE I

	DIRECT TESTING	PASSIVE TRANSFER	
		SENSITIZED SITES	CONTROL
Egg white	±	0	0
Egg yolk	++++	++	0
Chicken meat	0	0	0
Sterile salt solution	0	±	±
Yellow-fever vaccine dilution 1:100	++	+	±
Triple typhoid vaccine dilution 1:100	0	±	±
Typhus vaccine dilution 1:100	++++	++	±

COMMENT

We feel that we have definitely established the fact that this soldier is sensitive to egg yolk and that his allergic manifestations were due to the inoculations of typhus-fever and yellow-fever vaccines. The yellow-fever vaccine is prepared from infected chick embryos while the typhus vaccine is prepared from infected yolk sacs. Plotz[7] states that experiments have shown that the typhus vaccine contains some egg yolk and egg ovalbumin and that it has been shown that egg sensitive individuals react either locally or with general symptoms when given egg vaccines.

Here again, we wish to stress the fact that individuals who are sensitive to egg or chicken, or both, may develop allergic manifestations from virus vaccines that are prepared from egg yolk or chick embryo. We further believe that this occurs more often than present reports indicate. Nevertheless, it is not the purpose of this paper to decry the efficacious use of these important prophylactic agents. Instead, we merely wish to report that allergic manifestations do exist in egg and chicken sensitive patients and that, once this fact has been established, it necessitates the cautious administration of the vaccine, by giving it in small increasing doses and by having epinephrine and a tourniquet on hand.

SUMMARY

1. Egg yolk sensitivity alone may exist without concomitant egg white sensitivity.

2. Individuals sensitive to egg or chicken may develop allergic manifestations from virus or rickettsial vaccines which are grown on egg yolk sacs or chick embryos.

3. The attention of the medical profession is invited to the allergic potentialities of these vaccines so that necessary precautions can be taken in their administration.

REFERENCES

1. Swartz, Harry: Systemic Allergic Reaction Induced by Yellow Fever Vaccine, J. Lab. & Clin. Med. 28: 1667, 1943.
2. Sulzberger, M. B., and Asher, C.: Urticaria and Erythema Multiforme-Like Eruptions Following Injection of Yellow Fever Vaccine, U. S. Nav. M. Bull. 40: 411, 1942.
3. Berge, T. O., and Hargett, M. V.: Anaphylaxis in Guinea Pigs Following Sensitization With Chick Embryo Yellow Fever Vaccine and Normal Chick Embryo, Pub. Health Rep. 57: 652, 1942.
4. Tuft, L.: Clinical Allergy, Philadelphia, 1938, W. B. Saunders Co.
5. Walzer, M.: Quoted by Vaughan, W. T.: Practice of Allergy, St. Louis, 1939, The C. V. Mosby Co.
6. Feinberg, S. M.: Allergy in Practice, Chicago, 1944, The Year Book Publishers, Inc.
7. Plotz, Harry: Personal communication.

ADDENDUM

Subsequent to the writing of this paper a manuscript was received by this author from the Division of Virus and Rickettsial Diseases, Army Medical School, Washington, D. C., entitled "Allergenic and Anaphylactogenic Properties of Vaccines Prepared From Embryonic Tissues of Developing Chicks." This work is a complete and detailed study of this subject.

In this study Coulson and Stevens have unequivocally demonstrated experimentally that, although egg yolk and egg white contain antigens common to both, they also have antigens that are different and characteristic of only the yolk or the white, respectively.

Included in this paper, Stull presents further evidence that the presence of egg white and yolk antigens in egg embryo vaccine are of such quantity and specificity that they might produce dangerous systemic reactions upon injection in egg-sensitive individuals.

ANAPHYLACTIC SHOCK FROM SKIN TESTING*

Two Cases—One Fatal

Oscar Swineford, Jr., M.D., University, Va.

ANAPHYLACTIC shock and death in human beings have been reviewed by Vaughan.[1] Thomas and Fenton[2] have reported three deaths and four systemic reactions from pontocaine used in endoscopy. Sinapoidin caused shock in Phillips' case.[3] There have been two other reports,[4, 5] since 1938, of shock after intracutaneous injections. One recent death from 10 grains of aspirin will be reported separately. In 1941,[6] evidence was offered to support the belief that anaphylactic shock from skin testing was the result of exquisite sensitization to one or a few allergens rather than to the accumulated effect of numerous strongly positive reactions. A rapidly developing huge local reaction had, until then and later, given warning of each impending troublesome systemic reaction to skin tests or to injections of allergens.

Ratner[7] and Rowe[8] described anaphylactic shock from intracutaneous test injections from which there were negative local skin reactions.

The present report is of two cases, one fatal, which occurred before skin tests had become strongly positive.

CASE REPORTS

Case 1.—A white, married man, aged 49 years, had had asthma for four years. He also had had urticaria, poison ivy, and hay fever. Four severe asthmatic attacks occurred two weeks before admission after several months of comparative freedom from symptoms. The asthma was perennial with exacerbations in early spring and in October or November and was accompanied by purulent sputum and postnasal discharge. Adrenalin always had relieved previous attacks.

Mustard, catsup, mayonnaise, and cabbage caused distention and burning of the throat; dust from hay, feeds, grains, and house caused asthma and hay fever; temperature changes, dampness, exercise, and excitement caused wheezing.

The remainder of the history was irrelevant.

On physical examination the essential findings were a typically pale, boggy, and swollen nasal mucosa. Numerous asthmatic râles and ronchi were heard in the lungs.

Routine examinations of urine and Wassermann and Kahn reactions were negative. Blood examinations were not reported.

The day after admission, after a comfortable night, the patient was sent to the allergy laboratory for routine skin testing. He was wheezing moderately and was slightly cyanotic but was not acutely uncomfortable. Symptomatic treatment had been withheld that morning. Preliminary cutaneous tests with 72 commonly reacting allergens were negative. After 56 routine intracutaneous food extracts and eight or nine intracutaneous inhalant extracts had been injected he complained of not feeling well. There was no cough or dyspnea immediately. He was given two doses of adrenalin of 3 minims each. A tourniquet was applied

*From the Allergy Clinic, Department of Internal Medicine, University of Virginia Medical School, Charlottesville, Virginia.

above the test sites. Rather suddenly, in a minute or two, perhaps ten minutes after the tests were started, he started gasping for breath and became extremely apprehensive and cyanotic. Within another minute or two he was comatose. The time between his statement that he did not feel well and the advent of coma and extensive acute emphysema was not more than five minutes. He was given 0.5 Gm. of aminophylline intravenously, oxygen by nasal catheter, artificial respiration, and additional adrenalin. He was placed in the mechanical respirator. However, before aminophylline administration was completed, he seemed to be dead. His heartbeat could not be heard nor could his pulse be felt within fifteen minutes after he had entered the laboratory. He did not respond to any of the efforts to resuscitate him.

The catastrophe occurred before any of the five or six positive food reactions had become stronger than 1 plus or 2 plus. They did not get stronger, and there was no time to identify them. The few inhalants did not react. By the time the emergency measures had been completed the reactions had subsided. A post-mortem examination was not permitted.

CASE 2.—A white, married woman, aged 49 years, had had asthma, intermittently, for fifteen years. Attacks occurred about twice a month with no seasonal variation and were frequently associated with hay fever and urticaria. There was no sinus infection but there was some eczema of the face.

Asthmatic attacks followed ingestion of onions, tomatoes, and mustard; asthma, cough, or vasomotor rhinitis was induced by dust, chicken feed, horses, tobacco smoke, face powder, perfume, and roses; and asthma followed exposure to cold, exercise, fatigue, or excitement.

On physical examination, moderate wheezing obscured the heart sounds, the blood pressure was 125/80. Numerous other symptoms and physical signs were irrelevant. There were no foci of infection in ears, nose, or throat.

X-ray films of the chest were reported as normal. Routine studies of urine, stool, blood count, and Wassermann and Kahn reactions were normal.

Preliminary cutaneous tests with 72 commonly reacting allergens were negative. Fifty-six routine intracutaneous food extracts and 8 or 9 intracutaneous inhalant extracts had been injected when she complained of thickness of the tongue. Moderate wheezing began in one or two minutes. In another minute or two she became extraordinarily apprehensive and was thrashing about wildly. Dyspnea increased alarmingly. During the next two or three minutes, five 3-minim doses of adrenalin were given, one of them intravenously. She was given 0.5 Gm. of aminophylline intravenously. Within two or three minutes the respiratory difficulty was no longer alarming, but she continued to be apprehensive. She vomited several times and spat up large quantities of mucus. Immediately after administration of adrenalin and aminophylline, the blood pressure was 65/55 in the right arm. It remained between 65/55 and 80/65 until an intravenous saline infusion was started ten or fifteen minutes later. The blood pressure rose to 118/80 after 150 c.c. of saline had run in. The pulse, which had been about 130 beats per minute, slowed to about 100, and her chest became almost free from ronchi. She was returned to the ward where she relapsed into shock, with a blood pressure of 65/50, without appreciable asthma. Adrenalin in oil, ephedrine, and another infusion brought her out of shock promptly. Her recovery was uneventful.

Five or six intracutaneous food reactions could have been graded 1 plus or 2 plus when she became so ill that there was no time to identify them. By the time she seemed out of danger the local reactions had subsided. None of them became strongly positive. The few inhalants did not react.

Four days later scratch tests were done with all of the foods which had been injected intracutaneously originally. These gave weakly positive cutaneous reactions to American cheese, egg, vanilla, citrus fruits, rye, rice, beef, chicken, milk, pecan, English walnut, sweet potato, cucumber-squash-melon, cow hair, and feathers. There were strong cutaneous reactions to wheat, barley, lamb, lettuce-salsify, cabbage-cauliflower-kale-broccoli-brussel sprouts, beans, asparagus-onion, white potato-tomato, carrots-celery-parsnip, and olive. There was a huge cutaneous reaction to the group containing mustard-turnip-watercress.

There were strong intracutaneous reactions to mattress and rug dusts, asthma powders, cotton linters, *Pyrethrum*, *Fusarium*, and karaya gum. There were numerous negative, questionable, and weak cutaneous and intracutaneous reactions which need not be detailed.

After the huge cutaneous reaction to mustard, etc., she remembered that, when she worked in a restaurant, the other waitresses had had to handle dishes with mustard remnants on them because the taste, touch, or smell of mustard would cause asthma or a rash promptly. Because of this the shock was attributed to the intracutaneous test with mustard, although no attempt was made to prove it. The mustard-turnip-watercress group was not in the preliminary cutaneous test substances.

She was discharged from the hospital, symptom-free, on the usual initial program of avoidance of positively reacting foods and inhalants plus the use of dustproof mattress and pillow cases and symptomatic remedies.

DISCUSSION

The technique for testing these patients was the same as that used on about 7,000 patients in the past ten years—a total of nearly one million individual tests. Several other patients, after a huge prodromal local reaction, had had some urticaria or wheezing and one had had severe asthma after intracutaneous tests. Each, however, had been relieved promptly by adrenalin and a tourniquet above the local reaction.

These two experiences, plus those of Ratner[7] and Rowe,[8] have not altered our belief that constitutional reactions are the result of exquisite sensitization to one or a few allergens.

These severe reactions prove conclusively that a routine of scratch tests with 60 or 70 common reactions, as was then in use in this and other clinics, is an inadequate precaution against disaster. Every intradermal test should be preceded by the less sensitive scratch test.

SUMMARY

1. Two cases of anaphylactic shock from intracutaneous skin tests with food extracts are described. The food which caused the fatal reaction was not determined. The nonfatal reaction was thought to be due to mustard.

2. In both, anaphylactic shock occurred before there was time for the skin reactions to become strongly positive.

REFERENCES

1. Vaughan, W. T.: Practice of Allergy, St. Louis, Chap. 65, The C. V. Mosby Co.
2. Thomas, J. W., and Fenton, M. M.: Fatalities and Constitutional Reactions Following the Use of Pontocaine, J. ALLERGY 14: 145, 1943.
3. Phillips, E. W.: Allergic Shock, Caused by Synapoidin, Am. J. Obst. & Gynec. 44: 706, 1942.
4. Hunt, E. L.: Death From Allergic Shock, New England J. Med. 228: 502, 1943.
5. de Gregorio, E.: Anaphylactic Shock Due to Intracutaneous Protein Therapy in Two Cases of Pelada, Actas dermo-sif. 33: 138, 1941.
6. Swineford, O., Jr.: Skin Testing Methods, J. ALLERGY 12: 470, 1941.
7. Ratner, Bret: Allergy, Anaphylaxis, and Immunotherapy, Baltimore, 1943, Williams & Wilkins Company, p. 480.
8. Rowe, A. H., Discussion of: Waldbott, G. L.: Human Anaphylactic Shock. III. From Substances Other Than Pollen and Serum, J. ALLERGY 5: 219, 1934.

Special Reports

BRONCHIAL ASTHMA*†

A Critical Review

Louis Tuft, M.D., Philadelphia, Pa.

IF I WERE to make the following statements, namely: that bronchial asthma is a paroxysmal dyspnea which is the result of spasmodic contraction of the bronchial tubes, that there is some diversity of opinion as to its etiology, that it is associated with such nose and throat affections as enlarged tonsils or nasal polypi, and that other causes in susceptible persons include inhalation of certain odors or emanations, also exposure to certain flowers or plants, change of air, and purely emotional causes such as fright and emotion, I am sure that few would disagree with those statements. Yet they are excerpts from a textbook published nearly fifty years ago. I mention this only to emphasize that, while we have made progress in our understanding of asthma, it actually is not as great as many of us believe. Most of the advance has resulted from our researches, first in experimental anaphylaxis and later in human allergy. This knowledge has enabled us to explain in clearer, more scientific, and even in readily demonstrable fashion the exact causes of the asthmatic attacks. It also has been helpful both in diagnosis and treatment, serving, for example, to clarify more scientifically those impressions gained formerly only through clinical experience.

In spite of these advances, all clinicians whether old or new, have had to take care of asthmatic patients in whom the etiology is obscure and management exceedingly difficult. This has led to speculations and theories as to causation which are based more on clinical experience than on scientific facts and consequently have led to varied types of treatment. The logical result has been the building up of a highly controversial literature with marked difference of opinion especially regarding etiology and pathogenesis. I thought, therefore, that it might be worth while to attempt to review in critical fashion those aspects of asthma which are speculative in character. No attempt will be made in any way to review the literature on this subject no doubt already familiar to you, since it would serve no useful purpose. When possible, the prevalent views on the subject under discussion will be summarized. Most of what I have to say necessarily is based upon my own clinical experience with asthmatic patients. If this seems at times hypercritical, I trust that you will realize that it is offered with the hope that it may aid us in our knowledge of asthma and possibly stimulate renewed efforts toward the solutions of its many problems.

*Lecture given before the Seventh Annual Forum on Allergy, Pittsburg, Pa., Jan. 20, 1945.

†From the Clinic of Allergy and Applied Immunology, Temple University Hospital and School of Medicine.

In considering the etiology of asthma, no one can doubt the marked progress which our knowledge of specific sensitization or allergy has provided. Factors which were merely suspected by older clinicians of being causative in asthma, as, for example, animal emanations or odors, were clearly and scientifically proved to be due to specific sensitization to definite allergens. This was accomplished not only by means of specifically positive skin tests but by clinical tests as well. It could be shown without question that asthmatic attacks in certain patients were provoked by a specific antigen-antibody reaction taking place in or upon the cells of the bronchial mucosa and provoked by specific inhalant allergens such as dust, pollens, the animal danders, molds, etc., or by specific ingestants such as foods or drugs. The significance of such predisposing factors as constitutional susceptibility or environmental contacts in etiology, likewise, has been generally recognized and accepted.

Little difference of opinion exists, therefore, regarding patients in whom these specific provocative factors are found. Where the allergist is fortunate enough to prove the existence of specific sensitivity, diagnosis is easier, and the management of the patient likewise is simplified. Most of our difficulty is experienced with those asthmatic patients in whom no specific factor is ascertainable. This is the group which so frequently is labeled "intrinsic," "infectious," or "bacterial" asthmatics and in whom the etiology is ascribed to such factors as biochemical alteration, endocrine imbalance, bacterial allergy, or more recently to psychosomatic upsets.

This designation, in my opinion, is unwarranted in most instances. It is applied usually on no other basis than the inability to find a specific allergen as the cause of the patient's asthma, so that it actually is a cloak for our ignorance. It certainly is possible in such cases that the asthma is provoked by such unknown intrinsic factors as, for example, sensitivity to altered products of our own metabolism or even to bacterial sensitization. However, the proof of the existence of these factors is insufficient to warrant such a designation. Furthermore, the use of the terms "intrinsic" and "infectious" is determined not by definite evidence in the patient pointing to such factors, but rather by the inability to find any extrinsic factor as a basis. This is proved when patients considered as intrinsic or infectious are placed immediately in the extrinsic group as soon as the specific factor has been ascertained. It was the practice of older clinicians when confronted with conditions of unknown etiology (e.g., fevers, pupuric eruptions, etc.) to apply the term *idiopathic* to them to indicate that the cause had not as yet been determined. I believe we would do well to imitate that practice and speak of idiopathic asthma rather than to infer, by the use of such terms as "intrinsic" and "infectious," that we know the etiology in such patients.

There are several reasons for this tendency to classify asthmatic patients as intrinsic or infectious. One of these is the history of pneumonia, influenza, or pertussis prior to the onset of the initial asthmatic attacks. For some reason, the fact that asthma seems to follow one or more attacks of acute respiratory infections such as pneumonia seems to make it obligatory that it must be infec-

tious in origin. All of us know that these infections can act as trigger mechanisms in individuals who might just as readily develop hay fever as asthma if so predisposed. There would seem to be no more reason for assuming that the asthma in such instances is infectious than that the hay fever would be.

The roentgen-ray evidence of hyperplastic sinus disease in an asthmatic patient, even in an older patient, also is no valid reason for considering the asthma as infectious. It has been demonstrated definitely that similar findings can be discovered almost as frequently in nonallergic, nonasthmatic individuals. Furthermore, similar x-ray changes in the sinuses can be brought about by allergic edema of the mucosa and can give the misleading appearance of hyperplastic change. When the patient's condition improves, the disappearance of the swelling may, in turn, give rise to a normal appearance of the sinuses upon x-ray examination. A diagnosis of infectious asthma should not be made, therefore, upon x-ray evidence of sinus disease unless the latter has been shown definitely to be of the suppurative type.

The age of the asthmatic patient likewise is a frequent reason for classifying him as infectious or intrinsic. If a middle-aged or senile patient complains of asthma, and especially if it is of only a few years' standing, many of us almost immediately either consciously or unconsciously place him in the infectious category. If he happens to have an associated rhinitis or sinusitis as indicated by x-ray examination and if skin tests are indefinite, this assumption is strengthened, and he is treated accordingly. The ability to develop or show specific sensitivities to inhalant allergens and particularly to foods for some odd reason is considered to be a faculty reserved only for the young. No one denies that hay fever patients can and frequently do manifest their initial symptoms in middle life or later, but this is considered exceptional. It does not seem to nullify the golden rule; namely, that asthma in later life nearly always is of the intrinsic or infectious type.

It probably is true that asthma in younger individuals is more likely to be provoked by specific allergens, especially foods, than in older patients. Nevertheless, this does not preclude the existence of those allergies in the latter group. We all see asthmatic patients past middle life who are sensitive to house dust or other inhalants and even to foods. I frequently see older patients whose asthma disappears almost immediately after admission to the hospital because they are removed from the environmental allergens to which they were sensitive. The following case is an example.

A man, aged 68 years, was admitted to Temple University Hospital because of recurrent asthma of two years' duration. At the time of admission, he showed mild asthma which disappeared within twenty-four hours, even without the use of any medication. Cardiac examination was negative. Bronchoscopic examination showed the usual changes seen in asthma. Skin tests, except for slight reaction to dust, were entirely negative. Sinus x-rays showed some hyperplastic changes in the right antrum. The patient had a chicken farm in Maine and told us he always seemed better when away from it. He was completely free from asthma for the entire two weeks of his stay and required no treatment. He was discharged with the advice that he was not to return to his farm again but to change his residence to one more suitable.

There certainly is nothing about this case to suggest an infectious etiology. If the patient had been 28, instead of 68 years of age, no one would hesitate to classify him as having allergic asthma due to environmental allergens. There would seem no valid basis to change this viewpoint merely because of the difference in age.

Probably the most frequent reason for classifying asthma as infectious regardless of the age of the victim is a history of so-called "upper respiratory infection" just prior to the onset of the acute asthmatic attack. In many if not most instances in my experience, these in reality are allergic coryzas which are provoked by the same allergic factors as the asthma itself. These coryzal attacks usually not only precede the asthmatic attack but have been present in recurrent fashion for months or years prior to the onset of the asthma. The latter really represents the terminal phase of the untreated and unchecked allergic rhinitis just as it does in untreated hay fever. I have seen few allergic asthmatic patients, even of the advanced intractable type, in whom the asthma was not antedated by an allergic rhinitis often of long duration. The following case is an example.

A man, aged 57 years, was first seen in July, 1937, with recurrent asthma beginning at the age of 40 years. This, in the opinion of the referring physician, apparently was of infectious origin because of the accompanying sinus infection for which extensive local nasal treatment was being given. Examination revealed moderate emphysema, typical asthmatic breathing, and mild hypertension. Skin tests showed only slightly positive reactions to house dust and feathers and indefinite reactions to some foods.

Such a history certainly seemed, at the time, to justify the assumption that this was a case of infectious asthma. However, a more detailed history showed that, for years prior to the onset of the asthma, the patient suffered from repeated attacks of coryza with symptoms typical of the allergic type and had numerous polyps removed. Further observation of the patient indicated that whenever he went on a business trip to the south or on a vacation to Atlantic City, his breathing became normal whereas almost immediately after return to his home, it became worse. All local nasal treatment was discontinued, and he was treated like any patient with allergic asthma. In the past year, at the age of 64, he moved permanently to Atlantic City and has been quite comfortable.

Here then is a patient, formerly treated for infectious asthma but in reality having asthma of the ordinary allergic type, who like many other similar cases had a history of long-standing allergic rhinitis preceding the onset of the initial asthmatic attack. I quite often see asthmatic patients, especially in hospital practice, who are regarded and treated as infectious cases in whom a long-standing rhinitis either has been overlooked entirely or has been considered either as sinusitis, common cold, or as nasal catarrh and treated accordingly. If the patient did not have asthma, was in the younger age group, and gave a similar history, we immediately would suspect an allergic rhinitis and take proper steps to corroborate it. The fact that the patient has asthma, for some unknown reason, seems to make a difference and to exclude the possibility that the "colds" were, in reality, precedent allergic rhinitis rather than an infectious type. As a matter of fact, I have seen few allergic asthmatic patients whose asthma was not antedated by allergic rhinitis, often of long duration. If we would only take the time and trouble to go into the history more in detail and to make

additional examinations of the nasal mucosa during attacks and of the nasal secretions for eosinophiles, this error might be avoided. I stress the necessity for this differentiation because of the frequency with which it is overlooked; also because I am convinced that early recognition and proper treatment during this stage is the principal hope in the prevention of the intractable asthma which may follow.

Another important and frequent cause for confusion in diagnosis is the initiation or aggravation of asthma which takes place coincident with the change of seasons, in the spring about March or in the early fall during late September or early October, especially, in the latter instance, in fall hay fever patients. Because of the associated coryza which precedes or accompanies the asthma and since they occur at a time when upper respiratory infections are believed to prevail, it is assumed that both the rhinitis and the asthma are infectious in origin. Such assumption is not warranted by detailed study of some of these patients, which reveals that the attacks are allergic in character. Thus, the nasal symptoms consist of sneezing or nasal obstruction, or both with mucoid eosinophile-containing discharges; the asthma is paroxysmal, often mild and of short duration and occurs especially at night often at the same hour. The nasal or bronchial symptoms affect not only one patient but many of them and not only at the identical times of the year but even during the same hours. In some patients, the nasal symptoms predominate and the asthma is mild; in others, the asthma is prominent and may be quite severe. As one follows the course of these patients over the years, one finds that these periods of aggravation occur so precisely at the same time each year that if we were to plot a curve of attack rate, it would be found that the curve shows a sharp increase during these early fall and early spring periods not only for the single patient but for the entire group. This occurrence has been so common in my experience that if one asthmatic patient comes in during this period complaining of nocturnal wheezing, I can be sure that most of the other members of the same group will present similar complaints exactly at the same time.

I have puzzled for many years now over the possible explanations for this fall and spring aggravation. The regularity and uniformity of occurrence not only at a certain time of the day or week or year but also in so many other asthmatic patients, the short duration of the individual attacks, the absence of any signs of infection, and the resemblance of the symptoms and physical findings to allergic rhinitis and asthma, preclude the possibility that they are infectious in origin. I have long been satisfied that such was not the case and that another explanation must be sought.

It is true of course that the aggravation in some patients, particularly those whose asthma accompanies late hay fever and persists into the late fall or longer, can be attributed to various extra-pollen factors, which are believed to operate after ragweed pollen has disappeared from the air. Thus, undoubtedly some attacks can be attributed to increased exposure to inhalant allergens especially house dust, feathers, wool, or tobacco smoke coincident with greater confinement to the house or to the turning on of heat in the house or to exposure to irritants

like camphor, cedar, disinfectants, or to similar factors. This does not account, however, for most of the members of the group, especially those without antecedent hay fever, for those occurring in the early spring, and particularly for those in whom these inhalants do not appear to be of etiological moment.

For want of any more satisfactory explanation, I have ascribed these attacks to changes in the weather, especially in accounting for them to patients; however, I am firmly convinced that they are definitely related to some atmospheric or meteorologic change, the nature of which is unknown to us even though we are willing to classify it as a form of physical allergy. There are several reasons to support this feeling—thus the symptoms disappear at once following change to a warmer climate and recur immediately upon returning to the cooler area. I have had many Philadelphia patients, whose nasal or bronchial symptoms disappeared when the train reached Virginia on their way to Florida and reappeared on the return trip as soon as the train got north of Washington, D. C., to a cooler atmosphere. I thought perhaps these characteristics were peculiar only to the changeable climate of the Philadelphia area during the fall and spring months. However, after discussion with allergists in other localities, I learned that similar exacerbations affect patients in those areas not only in this country but in places like Havana and even in the Southwest Pacific. Physicians in Army hospitals tell of asthmatic patients returning from the Southwest Pacific who would have sudden acute attacks just before the onset of one of the unexpected tropical storms prevalent in those areas. These attacks would cease immediately after the sun came out. All of us have seen similar patients with allergic rhinitis, or asthma, or both who, almost like the rheumatic patient, could anticipate rainfall by several hours because of the development of a coryza, or a stuffy nose, or by heaviness in the chest or wheezing. These symptoms would disappear usually as soon as the weather cleared. There certainly could be nothing about such attacks to indicate that they are infectious in origin and no reason to explain such exacerbations upon that basis.

It is of course not unlikely that the atmospheric factor combined with that of extra pollen sensitivity, may account for the fall prolongation of asthma occurring in hay fever patients. This is supported by the fact that asthma occurs much less frequently in grass-sensitive patients and rarely is prolonged beyond the pollinating season. Such a difference becomes readily explanable because we have a period of warm and reasonably stable weather following the grass season, in contrast to the unstable cooler period which follows the fall hay fever season.

Unfortunately, little is known about the nature of these atmospheric changes or why some individuals are affected to a greater extent than others. Nevertheless, until we learn more about these things, it seems preferable to continue to attribute them to weather or atmospheric changes rather than to ascribe these symptoms to infection.

Despite my belief in the abuse of the terms "infectious" and "bacterial" as applied to asthma, this does not preclude the possible existence of bacterial sensitization in some asthmatic patients. One can reasonably assume that the respiratory mucosa, especially the bronchial portions, could lend itself in pre-

disposed patients to sensitization by bacteria or their products after repeated exposure such as might occur from upper respiratory infection. Difficulty arises when one attempts to determine the frequency with which this occurs and, as already indicated, it is given as a cause much more frequently than is warranted. Unfortunately, we are handicapped because there is no satisfactory way of determining definitely the existence of bacterial sensitization in such patients. Bacterial skin tests are extremely unreliable and nearly always nonspecific, and circulating antibodies are not demonstrable. Hence, most of the evidence is clinical in character, subject to wide variation and therefore open to considerable criticism.

Response to treatment whether by vaccine or by local or surgical treatment of the affected sinuses, certainly cannot be accepted as scientific proof of an etiological relationship because of the impossibility of ruling out nonspecific effects. Until more definite proof is furnished by subsequent research, one can only admit that bacterial sensitization may occur in asthmatic patients even if it cannot be definitely proved.

Before dismissing this subject, I would like to say something about the pathogenesis of asthma. An argument frequently advanced in support of the intrinsic nature of asthma is that removal of all causative allergens either from the diet or environment of the patient or putting the patient in an allergen-free chamber fails to relieve the asthma. It is assumed from this that extrinsic allergens therefore could not have been of significance, otherwise their removal would have been followed by relief. What is overlooked in these patients, however, is that the continued attacks in the "intrinsic case" is merely the end result of long-standing allergy with attacks taking place over a period of many years. Long-continued observation of these patients at various ages and different stages of the disease impresses one with facts about the pathogenesis or mechanism of development that serve, I believe, to explain rather clearly the reason for the chronic asthma. As previously indicated, allergy involving the respiratory tract nearly always affects the nasal mucosa first. This may be a defense mechanism designed to protect the bronchial tubes and lungs. If the attacks are repeated often enough and are of increasing severity, the lungs will be affected sooner or later. This is well illustrated in pollen hay fever; here the nose is attacked primarily and the bronchial shock organ only secondarily by asthma either after the patient has had it for a long time or when the amount of pollen in the air is so great that the nasal mucosa cannot protect the bronchi against it. Similarly in asthmatic patients, the nasal mucosa protects against asthma by a reaction in the form of repeated attacks of nasal allergy. As long as the reaction is confined to the nose, little damage is done and the bronchi are unaffected. However, if the nasal attacks continue in increasing severity, then, sooner or later, the bronchial shock organ is affected, and recurrent asthma results. These at first usually are intermittent and acute, are provoked by external allergens, and, in many patients, can be prevented by removal of these allergens or by protection against them. Such patients show little change in their lungs or chest even after many years of similar recurrences. However, in other pa-

tients each attack is accompanied by some change in the bronchial mucosa similar to that found in the nasal mucosa. With increasing frequency and severity of attacks these changes become more marked. Eventually they may overshadow the nasal picture so completely that the asthma becomes more prominent and more or less continuous. Emphysema of varying degree and bronchial inflammation then ensue and symbolize the end result of a process that has taken not months but usually years to bring about. Under those circumstances, it is no more logical to expect that removal of the offending allergen will relieve such patients than to expect the removal of infected tonsillar tissue to cure a rheumatic heart although the latter may have been caused originally by the streptococci contained in the tonsil tissue. Once the damage has been done whether in the patient with the rheumatic heart or, similarly, with the intractable asthma, it is futile to expect that removal of the offending agent necessarily will relieve the condition. Many of the so-called intrinsic asthmatic patients belong in this category and are the end result of long-standing preceding allergy. One might argue, of course, that the continued asthma may be the result of bacterial sensitization but, as already indicated, this is purely hypothetical and does not detract from the thought that basically such patients are allergic. It also seems unnecessary to postulate in such cases the existence of any unknown mechanism or "X" substance to account for their causation. Likewise, if such patients are considered as allergic in character and treated accordingly, one sometimes may be agreeably surprised by the favorable response obtained. Take, for example, the following patient:

A man, aged 62 years, was first seen in October, 1942, with chronic recurrent asthma present apparently since January, 1942. Subsequent, more detailed history revealed the presence of recurrent coryzal attacks since 1924. He was studied in another hospital in March, 1942, where a diagnosis was made of asthmatic bronchitis and moderate pulmonary emphysema with a suspicion of bronchiectasis. His tonsils were removed, a vaccine prepared and injections of it given, but his condition became increasingly worse. When first seen by me, the patient was in marked asthma, and I advised hospitalization. He wanted to defer this for a while so I gave him temporary relief with adrenalin, placed him on a diet excluding the more common offenders and prescribed small doses of iodides and aminophylline by mouth. Upon his return the following week, the improvement was indeed remarkable; he had practically no wheezing and remained relatively free for the balance of the winter, except for some coryza and wheezing after taking codeine or when in contact with dust or cooking odors. Although retired, he was able to do light work in a defense factory for eight hours daily without much difficulty, beginning March, 1943, and working throughout the summer into the fall. During the late fall, with onset of cooler weather, he had a recurrence of symptoms which did not respond immediately to ordinary medication. He left for Florida at this time, was relieved almost as soon as he arrived and remained relatively free both during his stay and since his return in the spring of 1944.

Here then is an instance of a patient considered and treated as infectious apparently because of his age and the recent onset of the disease, but who apparently had an allergic condition of the nose first with subsequent secondary involvement of the bronchi. When the patient was treated for allergic asthma instead of upon an infectious basis, he improved immediately.

So much then, for the etiology of asthma which I purposely have considered in detail. Space does not permit a detailed discussion of diagnosis, especially in

relation to methods. What might be said of these in other allergic diseases can be applied equally well to asthma. Too great reliance upon skin tests alone is to be deplored as well as the use of large numbers of tests without the proper interpretation of both positive and negative reactions. The failure to use adequate clinical and diet trial to corroborate the results of the allergic study likewise is to be decried. The thought that food allergy is unimportant in asthma, especially in adults, still seems to prevail in many quarters. The fallacy of this assumption can be readily ascertained by proper application of diagnostic methods to asthmatic patients and continued experience with them.

Turning now to a consideration of treatment, I find that there is much to commend and considerable to criticize about our present-day methods. In patients in whom specific allergens are found, excellent results can be achieved by the removal of these agents either from the diet or environment of the patients whenever this is possible. Indeed there is no more dramatic spectacle in medicine than the immediate relief obtained by the asthmatic patient who is sensitive to a cat or dog or specific food when these agents are withdrawn. It is the source of immense gratification to patients, their families, and to allergists and represents the goal toward which we all aim with other asthmatic patients. Even when it is not possible to eliminate contact with the offenders completely as in dust, pollen, or mold sensitive patients, it still is possible to provide some benefit by desensitization with extracts of these agents over a long period of time. While such patients do not always respond completely to treatment, nevertheless, they do fairly well as a group and, on the whole, provide relatively little difficulty. In many of these patients, dust desensitization is frequently instituted and often bacterial vaccine as well. While these agents are undoubtedly valuable in many patients, attention should be called to their frequent abuse. Since positive skin reactions to house dust extract are obtained so commonly in asthmatic patients, many practitioners inject both them and those with allergic rhinitis with dust extracts even without any preliminary testing. This is extremely unwise—I am sure that all of us have seen asthmatic patients whose conditions have been aggravated by overdosage with dust injections. This is true especially of young children. Only recently I saw an asthmatic child, 2 years of age, who had to be hospitalized for a week and put in an oxygen tent because of a severe attack that followed the second injection of a concentrated dust extract. Due care should be exercised in the use of such potent extracts especially in children. They should be employed only when there are proper indications for their use so that the consequences of overdosage may be avoided. This applies with equal force to bacterial vaccines whose use likewise is abused particularly in children. On more than one occasion I have been given credit undeservedly for a successful outcome when actually the patient's improvement resulted solely from the discontinuance of injections of dust or vaccine which had been given previously. I know too that not infrequently I had been guilty of inducing an asthmatic recurrence in a patient until I realized this by substituting buffered saline at the subsequent visits.

In spite of these drawbacks, the asthmatic patients with specific sensitivities present little difficulty in treatment. As already noted, the group presenting

most trouble is the one which includes patients in whom the etiology has been undetermined (the "intrinsic" or "infectious" group) the chronic asthmatic patient who goes from doctor to doctor or clinic to clinic seeking relief. It is this group which as a consequence are subjected to all sorts of nonspecific therapy and to every new device or nostrum that is introduced. Each year brings a new crop of remedies that is eagerly seized upon for trial in the intractable asthmatic patient who failed to respond to the previous year's panacea. I do not propose to attempt to review all of these as it would serve no useful purpose. Roentgen-ray therapy recommended again recently with favorable prospects has proved disappointing in our hands in a limited trial. I have used histamine rather extensively, particularly in those asthmatic patients with aggravations due to weather or to atmospheric changes, but cannot say that it has brought about any unusual benefit, chiefly because it has been employed along with other measures. The use of fever therapy, sulfanilamide, penicillin, and other nonspecific measures likewise has been tried in patients who failed to respond to other methods but with no great amount of success. Bronchoscopic aspiration has been employed by us in many patients with intractable asthma. It is, at times and for some unexplainable reason, followed by surprising relief and is worthy of trial. The aspirated secretion may then be used for the preparation of an autogenous vaccine which may be beneficial in these patients.

It is to be noted that I have said nothing so far about the treatment of infected sinuses in asthmatic patients. From what I have said previously it is obvious that I do not believe that sinus infection plays an important role in the etiology of asthma. I feel that the hyperplastic type found present so commonly in these patients is in reality part of the disease picture. Similar changes exist not only in the sinuses but in the mucosa of the entire respiratory tract. To remove this tissue merely from the paranasal sinuses and leave similar tissue in other portions of the respiratory mucosa does not seem logical since, if the asthma is the result of bacterial sensitization, the latter still will be provoked and continued from the other residual tissues. One might not object to minor operations done to relieve marked obstructions caused by large polyps or extensive septal deformities or to drain suppurative cavities. However, I have never been able to see the rationale of radical sinus operations on hyperplastic paranasal sinuses and seldom have recommended it. As a matter of fact, I became prejudiced unfavorably early in my experience with asthmatic patients because I seldom saw any benefit after these operations were performed. In fact it was the direct cause of death in one of my patients—a man, 53 years of age, whose life I am sure might have been prolonged by present conservative methods of treatment. Furthermore, in many other patients, asthmatic recurrences followed the repeated washing of the antra in an effort to clear up a supposedly existing infection. Since nasal treatment seemed only to do harm and produced little or no good, I made it a rule that no asthmatic patient have any local or other type of nasal treatment unless absolutely essential. I have even interdicted in many instances, the use of nose drops which likewise have been greatly abused. I must say that in the ten-year period since I adopted this prac-

tice, there has been little cause for regret. While I have no statistics to offer in substantiation, I am sure that these patients have fared better than those who previously were subjected to nasal treatment. From what I can gather from the literature and the experiences of others, I feel certain that our results have been as good and perhaps even better than in those asthmatic patients subjected to radical sinus surgery of repeated local nasal treatment.

It might be said in protest and probably with justice that such a conservative program of treatment offers little hope for the chronic asthmatic patient who fails to respond to specific or nonspecific methods of treatment. The truth of the matter is that in the present state of our knowledge we do not have much to offer to such patients at least in terms of cure. Much depends upon our attitude and upon what we expect to accomplish. For some curious and unexplained reason, many allergists do not seem satisfied with anything less than complete relief of the asthmatic patient. Possibly this is because of his experience with patients who get such dramatic results after removal of a cat or dog or a specific food. This is an ideal which all of us would like to attain but unfortunately it is possible only in a relatively small percentage of patients. It seems paradoxical to me that we should expect a 100 per cent result in asthma and yet are satisfied with much less in other allergic diseases. Thus, in hay fever where the etiology is easily ascertained and specific treatment readily instituted, we usually are content if the patient gets sufficient relief so that he has only a few bad days and mild symptoms in between. It seems to me that we should not expect any more of asthma. If some are fortunate enough to be completely relieved, well and good; however, if by appropriate measures, specific or otherwise, we can keep them from having any bad attacks and they are fairly comfortable at other times, this really is as much as one can expect. I believe it extremely important to tell asthmatic patients at the outset that they may have a little asthma from time to time or even an occasional more severe attack; however, they might be assured that it will be readily controlled by some type of drug therapy, either vaporized adrenalin, ephedrine, aminophylline, or similar drugs. They must be told that like the diabetic, the cardiac, the peptic ulcer patient, they too are readily susceptible to upsets upon the slightest provocation and after the least deviation. I find this assurance particularly necessary in those patients who have recurrences during periods of weather changes. We have little to offer these patients in the way of specific therapy. Some patients, particularly those who are pollen-sensitive, do improve sufficiently from specific treatment to overcome this tendency; in other cases dust or vaccine injections or even histamine may be beneficial. However, many others fail to be relieved and still have difficulty during these unsettled periods. Since climatic change is possible in only a small percentage, the balance will have to be treated by drug therapy until we are able to discover some method by which the allergic tissues of the respiratory tract can be made less susceptible to these influences. These patients need a great deal of reassurance to keep them from getting worse.

This type of treatment in such patients suggests that what we in reality are practicing is a form of psychotherapy. I must agree that it is, and that there

is a place for such treatment in the asthmatic patient. However, this does not prove that psychic factors or emotional upsets necessarily are the basic original causes of the asthma, as suggested in recent literature.

Attempts have been made to incriminate deeper, subconscious motives as responsible in certain patients as indicated by their response to psychoanalysis. In a condition as capricious and varying as asthma, it is hazardous to attribute any beneficial results in a few cases to any one procedure. No one will deny that psychic factors unquestionably can initiate an asthmatic attack in an allergic patient already predisposed to it from other causes. My objection is to the claim that the basis of the original attack is psychic in origin since there is little evidence to support such conclusion.

One factor which has not been stressed sufficiently especially in treatment is the importance of fear in the aggravation of asthma and the necessity for its proper control. Patients who first get an asthmatic attack react to it in a manner which might be as varied as the reactions of individuals to pain. Some years ago Libman pointed out that there was considerable variation in the manner in which patients reacted to pain; in some, it required a pain of great intensity to bring about any response; others would react in marked degree to even the slightest pressure. This is likewise true of patients during the throes of an asthmatic paroxysm. Some are little disturbed by even a severe attack and sort of take it in their stride. Others, however, become apprehensive even from a mild attack and feel that they are about to suffocate unless given instantaneous relief. They become excited, shout and moan, and upset everyone about them. These are the patients which interns and nurses in hospital wards and even the attending physicians label as neurotic, and who are relieved supposedly by sterile hypodermics to prove their point. Actually these patients even if they are of the emotional type should be given more attention than the asthmatic patient who suffers in silence. They really are badly frightened; hence, calm reassurance and, if necessary, sedatives properly applied will accomplish a great deal more than the commonly used methods of psychotherapy. This was expressed rather well recently by the reactions of a patient toward the latter type of treatment. She had been hospitalized for the second time because of an asthmatic recurrence, was quite upset emotionally, and created considerable disturbance in the ward during the attack. It was decided by the attending physician on ward service at the time that she was a neurotic; therefore a psychiatrist was called in. The latter proceeded to question the patient concerning her marital and sex relations with her husband and about similar matters in an attempt, apparently, to ferret out some hidden basic cause for the asthma. Consequently, there was no cooperation from the patient who remarked, and I thought intelligently, that she could not see why this had anything to do with her asthma—that when she began to get an attack she became very frightened and excited because she felt as if she were about to choke to death. All of us have seen this sort of thing repeatedly, I am sure, but the significance of the fear reaction is not always appreciated either by the attending physician or even by the psychiatrist who seems intent upon searching out more

hidden motives. It is this fear which prompts those patients who administer adrenalin to themselves to use it upon the slightest provocation since they are afraid of a bad attack. This is particularly true of patients who have previously had status asthmaticus—they are even more scared because each attack, though mild, brings with it the possibility that it might develop into another status attack.

Several years ago, I saw a man about 40 years of age who had rather severe asthma and had been hospitalized on several occasions in another city near his home for status asthmaticus. When he first consulted me, he showed considerable apprehension because of these previous experiences. Arrangements were made for his hospitalization, but this had to be delayed because of another status attack. On the day of his entrance to the hospital, he had a mild attack at his hotel. One glance at him showed the tremendous apprehension that he was about to go into another attack of status asthmaticus. Immediately after entering the hospital he was relieved by adrenalin and given a large dose of nembutal. He awoke the following day free from asthma. Following a complete study, a definite program of treatment was outlined, including measures which the patient could use to overcome mild attacks. He was acquainted with the fact that mild seizures were to be expected, but that appropriate measures would provide relief. When he left the hospital, he seemed to have lost his previous fears and apprehension. In the more than three years which have passed since then, he never had another status attack. Although he still has mild attacks from time to time, he is able to control them readily, is not incapacitated to any extent, carries on an active business, and seems to have lost his fear complex completely.

This case report exemplifies what I have seen in many other similar patients. It emphasizes the importance of fear in the aggravation of asthmatic attacks as well as the necessity for the institution of a type of "bedside psycho-therapy" formerly practiced so successfully by the old-time general practitioner whose presence at the bedside was sufficient to calm the patient. If we could only take enough time out from our busy practices to talk things over with asthmatic patients and to quiet their fears, such reassurances would accomplish a great deal more than what can be expected of prolonged psychoanalytic studies. I know from experience that it would aid materially in lessening the excitability of those asthmatic patients in whom the fear factor has become predominant.

In conclusion, I should like to say that, in spite of many deficiencies, even the practitioner who wrote about asthma a half-century ago would admit that we have made real progress in our knowledge of this condition. We have been able to demonstrate and prove scientifically its allergic character and to determine the cause in many cases to be specific sensitivity. Our greatest stumbling block still is the asthmatic patient in whom no specific allergen can be detected. Little is to be expected I believe from the designation of such cases as intrinsic or infectious unless future research provides more definite proof of the existence of such factors. It would seem preferable for the time being to continue the search for additional excitants as possible causes of the patient's asthma. Under the circumstances, I believe, too, that more will be accomplished if such asthmatic patients are regarded and treated as allergic until proved otherwise. If the "colds" or coryzas which either accompany or more often precede by months or years the asthmatic attacks were recognized early enough as allergic rather than as bacterial and appropriately treated, it would reduce

greatly the incidence of asthma especially of the intractable type. It constitutes, I am convinced, our best approach to prophylaxis in asthma. The most troublesome types, at least in my experience, are the climatic asthmas which are aggravated during periods of marked atmospheric changes and which so often are mistakenly treated as infectious in character. Nonspecific treatment will help some and is worthy of trial, especially if supplemented by measures providing symptomatic relief. However, until we can discover some means of altering the tissues of these patients so as to render them less reactive to atmospheric changes, they will continue to be the "problem children" of allergy, and many will require climatic changes as a permanent cure. These patients as well as others who do not respond satisfactorily to treatment require a type of psychotherapy readily applied at the bedside by the general practitioner or practicing allergist, namely a lot of reassurance to allay the fears which I am convinced are so important in the aggravation of asthmatic attacks. Finally, it should be pointed out that not infrequently in our enthusiastic attempts to rid the patient of his asthma quickly, we are likely to forget that treatment with such potent extracts as house dust or bacterial vaccines may aggravate the asthma as can be easily determined by discontinuing the treatment. On the whole, a conservative approach whether in relation to diagnosis or treatment, will eventually pay higher dividends in a condition which presents such vagaries and capriciousness as does asthma.

American Academy of Allergy

SECOND ANNUAL MEETING, CHICAGO, ILL., DEC. 10 AND 11, 1945

REPORTS OF COMMITTEES FOR YEAR ENDING DECEMBER, 1945

COMMITTEE ON EDUCATION

The Committee on Education reports that it has continued its interest and study in the three fields of education, undergraduate, graduate, and postgraduate, in spite of handicaps imposed by the times.

In undergraduate education the subcommittee, of which Dr. Swineford is chairman, has continued investigation of the teaching of Allergy in the medical schools of the United States. The results of his study and his ideas for improvement have been given to you in his Presidential Address. This will be published and needs no further comment here save to echo his feeling that Allergy is inadequately taught in the majority of schools. Methods for its improvement are being formulated, but it is a difficult matter with the degree of pressure which exists on the teaching staff of all medical schools.

In graduate education is included that of internes, residents, and fellows. It is assumed that graduates who wish to enroll for such work in the special field of Allergy contemplate certification by an appropriate Board, as Medicine, Pediatrics, etc. This means that they must conform to the requirements already imposed by such boards before they undertake work in a more restricted specialty. In other words, as expressed by the Secretary of the American Board of Internal Medicine, "The present regulations of the Board require three years of formal training in a residency or fellowship approved by the Council on Medical Education or under the immediate supervision of a preceptor in the field of general internal medicine. One year may be satisfied by an advanced degree in the basic sciences or by an approved residency in Pathology or by an approved residency in the subspecialties of medicine," of which Allergy is one. Since residencies and fellowships are not available upon graduation, this means that a minimum of twelve to eighteen months is required for internship training.

Physicians do not need certification in order to practice good medicine or pediatrics or allergy. Educational opportunities in Allergy for well-trained physicians must be created for those who, for various reasons, do not desire or need a certification status.

What seems needed then are two types of courses in Allergy, (1) the long term resident fellowship for one to two years, and (2) sound and well-organized short courses of instruction of variable duration.

Of the former there are about twenty, most of which are filled, but some should become available in six to twelve months.

The latter type of special instruction constitutes postgraduate education which should occupy an important part of our effort.

There are several types of courses that may be provided: (1) one week to two weeks —lecture course (basic or advanced), and (2) four to six months—clinical course. This is not feasible in the immediate future, but desirable as soon as possible.

Any or all types of courses should be given in all parts of the country at selected strategic points. The chief difficulty is to secure a group of teachers under existing conditions, but that situation should improve rapidly during the coming year.

During the past year several short courses have been given under the auspices of the Academy, or by Fellows of the Academy under other auspices such as the University of Pittsburgh, Columbia University, and the American College of Physicians. The fees returned from these courses, over and above expenses, are deposited with the Academy and set aside for educational purposes. At present this fund amounts to about $4,500.00.

For the coming year short courses are planned for:

January—New York Post Graduate Hospital—Dr. W. C. Spain directing.*

February—Massachusetts General Hospital, Boston—Dr. F. M. Rackemann directing.

March—New Orleans—details on page 47.

November—Roosevelt Hospital, New York—Dr. R. A. Cooke directing.

The February and November courses are being arranged by the American College of Physicians, but Members and Fellows may have the privilege of registration through the office of the American College of Physicians. Plans are under way for more extensive distribution of courses which will be announced as they mature.

In addition to these activities the Committee arranges for observational instruction of one to four months for physicians, especially those from South America who have been referred by certain bureaus of the Institute of International Education and the Pan-American Association. Most of the students have taken the short courses available to them during their visit.

The demand for opportunities in instruction is very heavy among veterans being separated from the Armed Forces. How to meet these requests is a serious problem.

If those established in practice who have opportunities in office or clinic will keep the chairman informed of vacancies as they occur, it will facilitate the proper disposition of these men. There seems to be no other way in which this information may be obtained.

Committee on Pharmaceuticals and Medicaments

The essential feature of the report was a recommendation for removal of advertising of the preparations, "Torantil" and "Hapamine" from THE JOURNAL OF ALLERGY. It was also announced that the committee recommends that the reports on "Hapamine" and "Torantil" which have been so carefully worked out by Drs. Simon and Squier be sent to each member and fellow of the Academy in the form of a mimeographed copy.

Constitution Committee

Dr. Feinberg requested a change in the method of application for membership, which is now cumbersome, in that instead of each application for membership being sponsored by three Fellows of the Academy, it be required that only one Fellow need act as sponsor. In addition, the applicant is to supply the names of three physicians in his community who can be used for reference regarding his ethical and professional attainments. This request was put in the form of a motion, put to a vote, and passed.

Dr. Feinberg also announced that the Constitution Committee had under consideration the addition of a group of men to be known as "Affiliate Members." These men would not necessarily be physicians, but those who occupy a high position in the sciences related to Allergy and who lend their efforts to the furtherance of our specialty.

Advisory Committee on Certification

During the past year this committee has acted in the field of certification solely as advisor to the American Board of Internal Medicine on matters pertaining to Allergy. As of Dec. 4, 1944, the Secretary of the Board of Internal Medicine reported that seventy-five physicians, previously certified in Internal Medicine, had been certified in Allergy with or without examination. During the year 1945 twelve have been approved by the Advisory Committee for admission to examinations by the Board of Internal Medicine. Five of these have been certified. The other seven have not yet been reported on, presumably because they have not taken the examinations.

The American Board of Pediatrics, Inc., has this year completed its plans for certification in Allergy of diplomates of their board. Notice of this step was released for publication to medical journals on September 18 and has appeared in the *Journal of the American Medi-*

*Registration for the course at New York Post Graduate Hospital may be made now through Dr. Spain.

cal Association. It has appeared in the November issue of THE JOURNAL and need not be incorporated here. Applications may now be made to the Secretary of the American Board of Pediatrics, Inc.

The plan is essentially the same as that adopted by the Board of Internal Medicine. The Advisory Committee on Allergy of this, the American Academy of Allergy, which now functions with the Board of Internal Medicine, has been appointed as the advisor to the Board of Pediatrics. As of this meeting, Dr. Oscar Schloss has been nominated to replace the retiring member of the Advisory Committee so that the Board of Pediatrics will receive immediate representation.

The Advisory Committee would like to recall to your mind the fact that this committee of the Academy acts only in that capacity which its name implies. It recommends applicants for examination and assists in the examination only insofar as Allergy is concerned, but the Board of Internal Medicine and now the Board of Pediatrics are free to accept or reject recommendations of this Advisory Committee.

The Advisory Committee has outlined certain requirements of study in preparation for the examination in Allergy which they believe are wise, but there is considerable flexibility in these suggestions. These recommendations were published in the November, 1942, issue of THE JOURNAL.

The Committee believes that it expresses the general opinion of this Academy by the statement that, if Allergy is to maintain a place of dignity and respect in the field of medicine, it must accept the idea of organized medicine that Internal Medicine and Pediatrics are the broad basic fields and that Allergy, just as tuberculosis, gastroenterology, and cardiovascular disease, is a subspecialty in a narrower sphere. The broader basic training is a prerequisite and it is the duty of this Academy to support all efforts toward improving educational standards in Medicine and particularly in Allergy.

It behooves all younger physicians, if they aspire to a specialty status that will secure official recognition, to plan their careers so as to fulfill the requirements of the boards that are recognized by the American Board of Medical Specialties.

MERITS COMMITTEE

For the second year the committee declined to award the Abbott and Marcelle Awards, because in the committee's judgment there had been no outstanding papers for research projects of sufficient merit. It also announced that an effort will be made to change the stipulations regarding these awards, so that the funds may be used for the establishment of Fellowships, or other aids to those engaged in problems of research.

The Will Cook Spain Award was given this year to Dr. Frank Simon of Louisville, Ky., for his excellent paper, "The Allergenic Interrelationship of Epidermis, Blood Serum and Skeletal Muscle."

CREDENTIALS COMMITTEE

Fifty-six applicants were recommended for Membership, as follows:

APPLICANTS FOR MEMBERSHIP

Alter, R. H., 511 Wildwood Ave., Jackson, Mich.
Barach, Alvan L. LeRoy, 950 Park Ave., New York, N. Y.
Bacal, H. L., 4990 Isabella Ave., Montreal, P. Q., Canada.
Bacon, Dr. Lyle C., Los Angeles, Calif.
Bartlett, Dr. Lester L., Pittsburgh, Pa.
Beaty, Harold W., Wells, N. Y.
Burke, Mead, 122 W. Washington Ave., Madison 3, Wis.
Brown, Earl B., 39 West 55th St., New York 19, N. Y.
Bohner, C. B., 4544 Carolton, Indianapolis, Ind.
Claybon, Dr. I. H., 243 Doctors Bldg., Cincinnati, Ohio.
Courtwright, Lazarre John, Station Hosp., Camp Polk, La.
Cortez, Jose Louis, Tlacotalpam, 109 Mexico City, Mexico.
Dintenfass, Capt. Arthur, 6230 Old York Rd., Philadelphia, Pa.

Dieckman, Capt. Herbert, Route 3, Evansville, Ind.
de Gora, Paul F., 200 Pinehurst Ave., New York 23, N. Y.
Ehret, Francis E., 333 Linwood Ave., Buffalo 9, N. Y.
Feinsilver, Oscar, 83 Morningside Rd., Worcester 2, Mass.
Friedlaender, Alex. S., 1512 Eaton Tower, Detroit 26, Mich.
Friedmar, Sam, Toledo, Ohio.
Forster, N. K., 6608 Forest Ave., Hammond, Ind.
Greco, J. B., Rua Guarani 179 Belo Horizonte Minas, Brazil.
Gordon, John E., 565 East End Ave., Pittsburgh, Pa.
Grout, Gerald C., 1080 Fidelity Bldg., Dayton 2, Ohio.
Henry, Dell, 514 Thompson St., Ann Arbor, Mich.
Hinnant, Iredell M., 3380 Norwood Rd., Shaker Heights, Cleveland, Ohio.
Jennes, Sidney W., 107 Farmington Ave., Waterbury, Conn.
Klein, Rose H., 58 Flagg St., West Hartford, Conn.
Kurland, Leonard T., Baltimore, Md.
Levin, I. Leonard, 606 Broadway, Lorain, Ohio.
Lilien, Adolph A., 133 E. 58th St., New York, N. Y.
Lowell, Francis Cabot, Garfield Rd., Concord, Mass.
McGrath, Robert Sterling, 1832 Eye St., N. W., Washington 6, D. C.
Merksamer, David, 105 Lincoln Rd., Brooklyn, N. Y.
Mendelsohn, H. Victor, 175 West 79th St., New York, N. Y.
Mauser, C. L., 2960 Piedmont Ave., Berkeley 5, Calif.
Morton, Major Wallace, Brooke General Hospital, Fort Sam Houston, Texas.
Merrill, George, 816 Ocean Ave., Brooklyn, N. Y.
Neidorff, A. Harvey, 1112 13th Ave., Altoona, Pa.
Ogden, Henry D., 626 Canal Bldg., New Orleans 12, La.
Palay, Lewis, 541 Lincoln Rd., Miami Beach 39, Fla.
Payne, Russell C., 1801 Eye St., N. W., Washington, D. C.
Rubin, Nathan Albert, 908 Colonial Blvd., Canton, Ohio.
Rostenberg, Adolph, Jr., University of Illinois, College of Medicine, 1853 West Polk St., Chicago 12, Ill.
Rawling, Frank F. A., 316 Michigan St., Toledo, Ohio.
Rotor, Arturo B., 1617 Massachusetts Ave., N. W., Washington 6, D. C.
Schulze, Victor E., Christoval Rd., San Angelo, Texas.
Scolten, Adrian H., 157 High St., Portland, Me.
Small, Willard, 98 North Madison, Pasadena 4, Calif.
Spiegel, B. Edgar, 25 Central Park West, New York 23, N. Y.
Stenbuck, Frederick A., 182 Park Ave., Mount Vernon, N. Y.
Targow, Abram M., 2007 Wilshire Blvd., Los Angeles 5, Calif.
Weiner, Harry, Los Angeles, Calif.
Wilson, Keith S., 4952 Maryland Ave., St. Louis, Mo.
Youman, J. Dudley, Jr., 1560 Line Ave., Shreveport, La.
Zoss, Albert R., 243 Doctors Bldg., Cincinnati, Ohio.
Zonis, Jonathan, 690 Newton St., Brookline, Mass.

These men were elected to full Membership in the American Academy of Allergy.

Six men were recommended for elevation to Fellowship in the Academy as follows:

PROPOSED FOR FELLOWSHIP

Garver, William P., Rose Bldg., Cleveland, Ohio.
Harten, Max, 135 Eastern Parkway, Brooklyn 17, N. Y.
Metzger, Frank, Tampa, Fla.
Rubin, Simon S., 707 Gary National Bank Bldg., Gary, Ind.
Schwartz, Emanuel, Brooklyn, N. Y.
Moore, Merle, Portland, Ore.

These men were elected to full Fellowship.

Pollen Survey Committee

During the past year an apparatus had been distributed to about a dozen members of the society for the purpose of obtaining a standard pollen count. The apparatus had proved quite satisfactory, except in a few minor respects, and during the coming year an effort will be made to enlarge the scope of the National Survey.

Obituary Committee

The deaths of Dr. Aaron Brown of New York and Dr. Abraham Trasoff of Philadelphia, which had occurred during the year, as well as that of Dr. Rudolph M. Hecht, who lost his life during the performance of his duty with an Army base hospital in France in 1944, were announced. Appropriate obituaries of Dr. Brown and Dr. Hecht have been printed in The Journal. Dr. George I. Blumstein read the obituary of Dr. Trasoff.

Treasurer's Report

The Treasurer's report was audited by Howard I. Hausman, Pittsburgh, Pa., and found correct.

STATEMENT OF RECEIPTS AND DISBURSEMENTS

Dec. 1, 1944, to Dec. 1, 1945

Receipts:	
December, 1944, from Dr. Spain for dinners at Waldorf	$ 1,965.00
December, 1944, for additional dinners at Waldorf	127.51
1945 Dues	4,356.50
Interest on U. S. Gov't Bonds	40.46
Grant from Marcelle Cosmetics	500.00
Grant from Almay Company	500.00
Fees from Allergy courses (as per enclosed schedule)	5,154.28
Total Receipts	$12,643.75
Disbursements—as per enclosed schedule	5,434.91
Net Receipts	$ 7,208.84
Initial Balance received Jan. 2, 1945, from Dr. Figley	1,802.88
Total Cash in Bank	$ 9,011.72
Cash Balance in Pitt National Bank	$ 9,011.72

SCHEDULE OF DISBURSEMENTS

Dec. 1, 1944, to Dec. 1, 1945

Secretarial Services:		
Dr. Spain	$ 55.00	
Dr. Figley	300.00	
Dr. Criep	110.00	$ 465.00
Franklin Printing & Engraving Company		323.32
Toledo Printing Company		269.18
C. V. Mosby Co.—Publication, Journal of Allergy		246.08
Gilbert Mail Service		116.50
Postage:		
Dr. Spain	$ 77.82	
Dr. Figley	66.38	
Dr. Criep	27.00	171.20

December, 1944, Meeting Expenses:			
Refunds	$ 62.50		
Secretarial Prize	25.00		
Stenotype Company	111.68		
Walfdorf-Astoria	2,293,48		
Speakers (expenses and honorariums)	540.11	3,032.77	
E. A. Wright Company		75.67	
Pitt National Bank:			
Safety Deposit Box	$ 6.00		
Cashing Canadian Check	1.70	7.70	
Miscellaneous Stationery		18.77	
Dr. Karl Figley—filing case		49.96	
Pittsburgh Allergy Course—as per enclosed schedule		633.76	
Howard I. Hausman—Public Accountant Fee		25.00	
Total Disbursements			$5,434.91

SCHEDULE OF ASSETS

Dec. 1, 1945

Cash Balance in Pitt National Bank			$ 9,011.72
Dues Receivable:			
1 Fellow	$ 20.00		
9 Members	135.00		
21 Servicemen	105.00		260.00
U. S. Government Bonds:			
2—$1000.00 Series F.	M966008F		
	M966009F		
2—$ 500 2½%	21721A		
	21722B		
Maturity Value			3,000.00
Total Assets			$12,271.72

The report was accepted. Following the reading of this report, Dr. Criep announced that the Executive Committee recommended that during the following year dues for Fellows be made $35 and dues for Members be made $25. He explained that this increase is quite necessary in order to keep abreast of the mounting expenses of the Academy. A motion to that effect was made and passed.

NOMINATING COMMITTEE

The following officers were recommended for the coming year:

President, Dr. Stearns S. Bullen
Vice-President, Dr. Will Cook Spain
Secretary, Dr. Karl D. Figley
Treasurer, Dr. Leo Criep

The Secretary cast an unanimous vote for the afore-named nominees, and the motion was passed.

(Signed)
KARL D. FIGLEY, M.D.
Secretary

A postgraduate course in Allergy is to be given by the American Academy of Allergy under the sponsorship of Tulane University and Louisiana State University School of Medicine at New Orleans, La., beginning Friday, March 8, 1945.

The course will take a period of five days with clinical demonstrations, lectures, and conferences. The fee is $40.00.

The faculty is to be composed of nationally known men, competent to discuss the various fields of allergy.

Those interested please address requests for information to The Committee on Local Arrangements, c/o Dr. Henry Ogden, Canal Building, New Orleans, La.

IN MEMORIAM

ABRAHAM TRASOFF
(1888-1945)

ABRAHAM TRASOFF died suddenly in Philadelphia, Nov. 24, 1945, in his fifty-sixth year. He was born on Dec. 15, 1888, and received his medical education at Medico Chirurgical College, graduating in 1915 He served as a Captain in World War I, and from 1919 to 1925 was consultant to the U. S. Veterans Bureau in Philadelphia.

He became interested in Allergy during its formative period. After taking a postgraduate course at the New York Hospital in 1927, he established the Allergy Clinic at Mt. Sinai Hospital in Philadelphia. He remained as head of this department until 1933, when he was elevated to the position of attending visiting physician, which he retained until his death. In addition, he was a member of the Philadelphia County Medical Society; Pennsylvania State Medical Society; a Fellow of the American Medical Association; Member and Past-President of the Philadelphia Allergy Society; a diplomat of the American Board of Internal Medicine with certification in Allergy; an associate member of the American College of Physicians; and a member of the American Academy of Allergy.

As a teacher, he stimulated his associates and guided them into the newer fields of medical science. He was profoundly interested in research and was always anxious to help anyone who sought aid in this field. He was a contributor to medical journals—both in the field of Allergy and General Medicine.

Abraham Trasoff was a fine physician in the true sense of the word, giving unselfishly of himself to those who needed it most. His humbleness, his altruistic nature, his sympathetic and understanding personality, and his keen intelligence and uncompromising integrity were but a few of his outstanding virtues.

The Academy mourns the loss of a well-beloved and respected friend and colleague and extends its heartfelt sympathy to his bereaved wife and children.

(Signed)
GEORGE I. BLUMSTEIN
LOUIS TUFT

DIRECTORY OF THE AMERICAN ACADEMY OF ALLERGY

(Continued)

MEMBERS OF THE ACADEMY

1940 **Alford, Ralph I.,** 83 Park St., Montclair, N. J.
b 1904. A.B., Princeton U. 1926; M.D., Columbia U. 1930; Major, M.C., A.U.S.; Chief, Allergy Sect., Percy Jones Gen. Hosp., Battle Creek, Mich.; Asst. Att. Phys., Mountainside Hosp., Montclair, N. J., and N. Y. U. Med. Sch., Allergy Dept.; F.A.C.P.

1942 **Alpher, Isadore M.,** 900 17 St., N. W., Washington 6, D. C.

1942 **Ancona, Giacomo R.,** 2000 Van Ness Ave., San Francisco 9, Calif.

1944 **Anderson, J. Mercer,** 509 1st National Bank Bldg., Salt Lake City 1, Utah.
b 1901. A.B., U. Utah 1922; M.D., Georgetown U. 1927; Cert. in Intern. Med. 1928; L.D.S. Groves and Salt Lake Co. Hosps.; A.M.A.; Utah State Med. Soc.

1944 **Baer, Rudolf L.,** 962 Park Ave., New York 28, N. Y.
b 1910. Basic Science Exam., Musterschule, Frankfort a.M., U. Heidelberg 1930; M.D., U. Frankfort 1933; Cert. in Dermat. and Syph. 1940; Asst. Att. Phys. and Postgrad. Teaching, Skin and Cancer Unit, N. Y. Post Grad. Hosp.; Jr. Asst. Dermat. and Syph., N. Y. Post Grad. Hosp.; Acting Assoc. Att. Phys. in Dermat. and Syph., Montefiore Hosp.; Asst. Vis. Phys., 3rd Med. Div., Coldwater Memorial Hosp.; N. Y. C. Dept. of Health; Consult. in Dermat., Monmouth Memorial Hosp., Long Branch, N. J.; F.A.A. Dermat. and Syph.; A.M.A., N. Y. Acad. Med.; M. Soc. Invest. Dermat.; Assoc. Allerg. Clin., Greater N. Y.; Assoc. Dermatosyph., Greater N. Y.; Adv. Ed. Bd., J. Invest. Dermat.

1940 **Baker, Arthur G.,** 107 E. Ridley Ave., Ridley Park, Pa.
b 1905. A.B., Swarthmore 1928; M.D., George Washington U. 1932; Clin. Asst. Allergy, Jefferson Hosp. and Germantown Hosp., Phila.; Consult. Allergy, Chester Co. Hosp., West Chester, Pa.; Asst. Demonst. Med., Jefferson Med. Coll.; A.M.A.

1939 **Beaver, Jennie A. D.,** 44 Elm St., Morristown, N. J.
b 1886. A.B., Cornell U. 1907; M.D., 1910; M., Sch. Health Assn.; A.M.A.

1944 **Bernstein, Clarence,** 740 N. Magnolia Ave., Orlando, Fla., also Winter Park, Fla., c/o Florida Sanitarium.
b 1905. B.A., Yale 1926; M.D., Johns Hopkins U. 1931; Cert. in Intern. Med. 1939 and Allergy 1944; Consult. Med. Staff, Fla. Sanitarium; Med. Staff, Orange Gen. Hosp.; Med. and Allergy Staff, Michael Reese Hosp.; Consult. in Med., Inst. Psychoanalysis, Chicago; Chicago Inst. Med.; M., Central Soc. Clin. Research; Chicago Soc. Intern. Med.; Chicago Soc. Allergy; Soc. Research in Psychosomatic Problems; Fla. Acad. Sciences; A.M.A.; A.O.A.; Sigma XI; Phi Beta Kappa.

1939 **Berresford, Arthur B.,** 608 E. State St., Ithaca, N. Y.
b 1903. E.E., Cornell U. 1929; A.B., 1931; M.D., Boston U. 1935; Allerg., Tompkins Co. Memorial Hosp., Ithaca, N. Y.; Research F., Roosevelt Hosp., N. Y. C.; A.M.A.

1944 **Blank, Philip,** 3028 Brownsville Rd., Brentwood, Pa.

1938 **Boker, Lilian A.,** 4622 Grosvenor Ave., New York 63, N. Y.
b 1904. B.A., Wellesley Coll. 1926; M.D., West. Reserve U. 1933; Asst., Ped. and Allergy and Asst., Allergy Clin., Roosevelt Hosp., N. Y. C.

1939 **Bolden, Arthur L.,** 4326 Spruce St., Philadelphia 4, Pa.
b 1904. Premed., Temple U. 1923; M.D., 1927; Cert. in Intern. Med. 1945; Asst., Allergy Clin., Jefferson Hosp.; Chief, Allergy Clin., Phila. Gen. Hosp.; Asst., Cardiac Clin., Graduate Hosp.; Demonst. Allergy, Jefferson Med. Coll.; A.M.A.

1942 **Bowen, Ralph,** 3509 Montrose Blvd., Houston 6, Texas.
b 1898. B.A., U. Iowa 1921; M.D., 1924; Cert. in Ped. 1936; Methodist, St. Joseph, and Memorial Hosps.; Assoc. Prof. Med., Baylor U.; F.A.C.A.; Southwest Forum Allerg., Pres., 1944; F.A.C.P.; Former F. A. A. P.; Founder and co-editor, Internat. Corresp. Club of Allergy.

1941 **Brier, Archibald J.**, 717 Mills Bldg., Topeka, Kan.
b 1892. B.S., Washburn Coll., St. Louis U. 1922; M.D., St. Louis U. 1924; Att. Staff, St. Francis, Christ's, and Stormont Hosps.; Consult. Allergy, A. T. & S. F. R. R. Assn.; A.M.A.; F.A.C.A.

1938 **Brown, Ethan Allan**, 75 Bay State Rd., Boston 15, Mass.
b 1905. Premed., Balliol Coll., Oxford; External & Internal Student, U. London 1928-1930; St. Mary's Hosp. Med. Sch., London; M.R.C.S. & L.R.C.P., London 1935; Phys. in-Chief, Allergy Dept., Boston Disp.; Consult. Allergy, Essex Co. Tbc. Sanatarium; Boston Floating and Pratt Diag. Hosps.; Instr. Med., Tufts Med. Sch.; A.M.A.; F.A.C.A.; Regent, 1942; M., A. Soc. Research Psychosomatic Problems; Soc. Invest. Dermat.

1939 **Brown, Fredrick R.**, 39 W. 55 St., New York 19, N. Y.
b 1911. A.B., Cornell U. 1931; M.D., 1934; Capt. M.C., A.U.S.; Asst. Clin. Vis. Phys., 3rd Med. Div., Bellevue Hosp.; Asst. Att. Phys. and Asst. Med. N. Y. U. Coll. Med.; Asst. Immunol., Midtown Hosp.

1940 **Brown, Lewis W.**, 160 Roseville Ave., Newark 7, N. J.

1939 **Brust, Raymond W.**, 4710 Chester Ave., Philadelphia 43, Pa.
b 1900. A.B., Holy Cross Coll. 1923; M.D., U. Pa. 1927; Vis. Phys. Phila. Gen. Hosp.; Clin. Asst., O.P.D. Immunol. (Asthma Clin.), Jefferson Med. Coll. Hosp.; Assoc. Med., U. Pa.; F.A.C.P. and Phila. Coll. Phys.; A.M.A.; M., Phila. Physiol. Soc. and Phila. Allergy Soc.

1941 **Bubert, Howard M.**, Med. Arts Bldg., Baltimore 1, Md.
b 1898. M.D., U. Md. 1920; Privileges, Md. Gen., Bon Secours, and Mercy Hosps.; Chief, Allergy Clin., Univ. Hosp.; Asst. Prof. Med. and Lect. Allergy, U. Md.; A.M.A.

1940 **Buffum, William P.**, 122 Waterman St., Providence 6, R. I.
b 1888. A.B., Brown 1909; M.D., Harvard 1913; Cert. in Ped. 1934; Chief, Ped. Service, R. I. Hosp.; Vis. Ped., Providence Lying In Hosp.; A.M.A.; F.A.A.P.; M., New Eng. Ped. Soc., Vice-Pres., 1940.

1940 **Byck, Louis**, 794 South 11 St., Newark 8, N. J.
b 1899. B.S., Coll. City N. Y. 1921; M.D., Columbia U. 1925; Capt., M.C., A.U.S.; Assoc. Phys. and Assoc. Allergy, Beth Israel Hosp., Newark; Chief Allergy Clin., Newark Memorial Hosp.; Allergy Clin., N. Y. Post Grad. Hosp.; A.M.A.

1941 **Chafee, Francis H.**, 12 Humboldt Ave., Providence 6, R. I.
b 1903. Ph.B., Brown U. 1927; M.D., Harvard 1931; Capt., M.C., A.U.S.; Vis. Phys., Dir. Allergy Clin., R. I. Hosp.; A.M.A.; F.A.C.P.; M., A. Federation Clin. Research.

1944 **Chait, Robert A.**, 1799 E. 14th St., Brooklyn, N. Y.
b 1909. B.S., Coll. City N. Y. 1930; M.D., U. Paris 1935; Cert. in Otolaryng. 1945; Capt., M.C., A.U.S.; Clin. Asst. in Otolaryng. and in Allergy, Brooklyn Jewish Hosp.

1944 **Claman, Leoni Neumann**, 40 East 88th St., New York 28, N. Y.
b 1901. B.S., Columbia U. 1922; M.D., 1924; Att. Phys. and Chief, Allergy Dept., N. Y. Inf. for Women and Children; Clin. Asst. Allergy, Roosevelt Hosp.; A.M.A.; M., A. Women's Med. Assn.

1944 **Clancy, James Francis**, 7258 Forest Ave., Hammond, Ind.
b 1900. M.D., U. Mich. 1925; Cert. in Ped. 1941; Maj., M.C., A.U.S.; St. Margarets Hosp.; F.A.A.P.; A.C.A.

1941 **Clapp, William B.**, 232 Worcester St., No. Grafton, Mass.
b 1906. A.B., U. Vermont 1927; M.D., 1932; Lt. Commdr., M.C., U.S.N.R.; Cert. in Intern. Med.; O.P. Staff, Mass. Gen. Hosp., Boston; O.P. and Staff, Worcester Memorial Hosp.

1942 **Cohen, Bernard J.**, Marlborough Apts., Baltimore 17, Md.
b 1904. Premed., U. Md., Johns Hopkins U. 1923; M.D., U. Md. 1927; Phys. Al-

lergy, Johns Hopkins Hosp.; Chief, O.P.D., Sinai Hosp.; In charge of Electrocardiography, Sinai Hosp.; Instr., Med. and Phys. Diag., Johns Hopkins Med. Sch.; A. Heart Assn.

1941 **Cohen, Victor L.,** 760 Potomac Ave., Buffalo 9, N. Y.
b 1904. B.S., M.D., U. Buffalo 1929; Maj., M.C., A.U.S.; Asst. Staff, Buffalo Children's, Mallard Fillmore, and Buffalo General Hosps.; A.M.A.; N. Y. State Branch, Soc. Bacteriol.

1944 **Colonnell, William J.,** 38-13 Bowne Street, Flushing, N. Y.
b 1904. A.B., Fordham U. 1925; M.D., N. Y. Med. Coll. 1929; Lt. Comdr., M.C., U.S.N.R.; Att. Allerg. & Immunol., Flushing Hosp.; F.A.C.A.

1944 **Conn, William V.,** 615 First National Bank Bldg., Greensburg, Pa.
b 1908. B.S., U. Pittsburgh 1931; M.D., Long Island Coll. Med. 1935; Vis. Phys., Westmoreland Hosp.; Clin. Asst., Dept. Med., Montefiore Hosp.; Instr., Dept. Med., U. Pittsburgh; A.M.A.; M., Pittsburgh Allerg. Soc.; Am. Pub. Health Assoc.; Pittsburgh Acad. Med.

1940 **Copeland, Solkin C.,** 1734 S. 58 St., Philadelphia 43, Pa.
b 1903. Premed. and M.D., U. Pa. 1927; Cert. in Ped. 1941; Allerg., Children's and Doctors' Hosps.; A.M.A.; Phila. Allergy Soc.; Phila. Ped. Soc.

1940 **Costigan, Thomas J.,** 50-34 41 St., Long Island City, N. Y.

1944 **Crandall, Frank G., Jr.,** 741 North Martel Ave., Los Angeles 46, Calif.
b 1896. M.D., U. Neb. 1921; Col., M.C., A.U.S.; Consult. Allergy, Los Angeles Orthopedic and Co. Gen. Hosps.; Dir. Allergy Clin. U. Calif., Los Angeles Med. Dept., Graves Memorial Dispensary, and Marion Davies Foundation; A.M.A.; Honorary Fellow, A.C.A.; Assn. Military Surgeons; M., Internat. Corresp. Club Allergy.

1941 **Crounse, Kenneth E.,** 501 State St., Albany 6, N. Y.
b 1897. A.B., Yale 1920; M.D., Albany Med. Coll. Union U. 1924; Asst. Att. Phys., Albany Hosp.; Instr. Med., Albany Med. Coll.

1942 **Davidson, Nachman,** 6100 Park Heights Ave., Baltimore 15, Md.
b 1910. A.B., Leigh U. 1931; M.D., U. Md. 1936; Lt., M.C., U.S.N.R.; University, Sinai, and West Baltimore Gen. Hosps.; Disp. Phys., Johns Hopkins Hosp.; Asst. Med., U. Md.

1941 **Dean, George Adgate,** 11 W. Church St., Fairport, N. Y.
b 1904. Premed., Cornell U.; M.D., U. Buffalo 1929; Lt. Comdr., M.C., U.S.N.R.; Phys., Allergy Clin., Genesee Hosp., Rochester, N. Y.; Asst. Phys., Allergy Clin., Strong Memorial Hosp., Rochester; Instr. Med., U. Rochester; F.A.C.A.; A.M.A.; M., Internat. Corresp. Club Allergy.

1941 **Derbes, Vincen Joseph,** 4478 Lafaye St., New Orleans 17, La.
b 1912. Premed. and M.D., Tulane Med. Sch. 1934; Charity Hosp.; Instr. Med., Tulane Med. Sch.; A.M.A.

1944 **Diamond, H. Elias,** 1749 Grand Concourse, Bronx 53, N. Y.
b 1901. B.S., C.C.N.Y. 1922; M.D., U. Md. 1926; F.A.C.A.; M. Internat. Corresp. Club Allergy.

1940 **Dundy, Harold David,** 1730 Carroll St., Brooklyn 13, N. Y.
b 1909. B.S., City College 1929; M.D., Bellevue Med. Coll. 1933; Clin. Asst. Ped. (Allergy), Post Grad. Hosp.; Assoc. Allergy, O.P.D. and Adj. Allergy, Bethel Hosp.

1941 **Durham, Oren C.,** Abbott Lab., North Chicago, Ill.
b 1889. Chief Botanist, Swan Myers Co., 1925-1930; Abbott Labs., 1930.

1940 **Ehrenfeld, Irving,** 185 Lexington Ave., Passaic, N. J.
b 1904. A.B., Columbia; M.D., N. Y. U. Coll. Med. 1930; Bellevue Hosp., N. Y.; Passaic Gen. Hosp.; Instr. Med., N. Y. U. Coll. Med.; A.M.A.

1941 **Epstein, Stephan,** 807 W. Fifth St., Marshfield, Wis.
b 1900. Premed. and Med., U. Erlangen, Heidelberg, 1923; Cert. in Dermat. and Syph. 1938; St. Joseph's Hosp., Marshfield; Extramural Staff, U. Wis.; A.M.A.;

F.A. Acad. Dermat. and A.C.A.; M., Soc. Invest. Dermat., Internat. Corresp. Club Allergy, Chicago Dermat. Soc., and Minn. Dermat. Soc.; Vice Pres., Minn. Dermat. Soc., 1943.

1939 **Fink, Arthur Irvin,** 724 W. North Ave., Baltimore 17, Md.
b 1897. A.B., Johns Hopkins U. 1923; M.D., 1927; Staff and in charge Allergy Clin., Sinai Hosp.; Phys., O.P.D., Johns Hopkins Hosp.; Instr. Med., Johns Hopkins Med. Sch.

1944 **Finkelstein, Manly,** 574 West End Ave., New York, N. Y.
b 1898. M.D., U. Manitoba 1921; Research F. Allergy, Roosevelt Hosp.; M., Nat. Soc. Gastro-Enterol.; A. Soc. Clin. Path.

1939 **Francis, Nathan,** 346 South Goodman St., Rochester 7, N. Y.
b 1897. A.B., U. Rochester 1924; M.D., N. Y. U. and Bellevue 1929; Capt., N.Y.G., 21st Reg.; Dir. Allergy Clin. and Assoc. Att. Phys., Rochester Gen. Hosp.; Sr. Att. Phys., Highland Hosp.; Phys., Allergy Clin., Genesee Hosp.; F.A.C.A.

1939 **Freedman, Barnett P.,** 322 George St., New Haven 1, Conn.
b 1896. Ph.B., Yale U. 1916; M.D., 1920; Asst. Att. in charge Allergy, Grace Hosp.; Asst. Allergy Clin., Jewish Hosp., Brooklyn; A.M.A.

1944 **Friedlaender, Sidney,** 737 W. Cornelia Ave., Chicago 13, Ill.
b 1915. A.B., Wayne U. 1935; M.D., 1938; Research F. Intern. Med., Northwest. U. Med. Sch.

1942 **Friedman, Harold J.,** 10515 Carnegie Ave., Cleveland 6, Ohio.
b 1907. A.B., Ohio State U. 1929; M.D., 1932; Mt. Sinai Hosp.

1940 **Fries, Joseph Harman,** 25 Plaza St., Brooklyn 17, N. Y.
b 1902. A.B., Columbia U. 1924; M.D., 1929; Cert. in Ped. 1940; Chief Allergy, Lutheran Hosp.; Assoc. Vis. Ped., Kings Co., Hosp.; Asst. Phys., Kingston Ave., Hosp.; Asst., Depts. Allergy & Ped., Brooklyn Jewish Hosp.; Instr. contagious diseases, L. I. Coll. Med. Sch.; Educ. Consult. Ped., Clin. Soc. Adj., N. Y. U. Coll.; M., A. Human Serum Assn.; Brooklyn Ped. Soc.; Assn. Allergy Clin. Greater N. Y.

1939 **Fromer, John L.,** 62 Marion St., Brookline, Mass.
b 1907. B.S., N. Y. U. 1929; M.D., 1932; Major, M.C., A.U.S.; Chief Allergy, Lovell Gen. Hosp.; Ft. Devens, Mass.; Lahey Clin., Boston; A.M.A.; F. A. Acad. Dermat.; St. Johns Hosp. Dermat. Assoc. (British); Boston Round Table Allergy.

1942 **Furman, Moses L.,** 1749 Grand Concourse, New York 53, N. Y.
b 1900. M.D., N. Y. U. 1924; Adjunct Ped. and Chief Ped. Allergy Clin., Bronx Hosp.; Asst. Allergy Clin., Flower Fifth Ave. Hosp.; N. Y. Med. Coll.; A.M.A.

1940 **Gaillard, George Everett,** Medical Centre Bldg., White Plains, N. Y.
b 1909. A.B., N. Y. U. 1932; M.D., N. Y. Med. Coll. 1936; N. Y. Post Grad. Hosp., N. Y.; White Plains and St. Agnes Hosps., White Plains; Teach. Staff, N. Y. Post Grad. Med. Sch. and Hosp.; A.M.A.

1944 **Gant, James Quincy, Jr.,** Dermatoses Section, National Institute of Health, Bethesda 14, Md.
b 1906. B.A., Ohio State U. 1930; M.D., Med. Coll. Va. 1935; Cert. A. Bd. Dermat. & Syph. 1943; Att., Dermat., U.S.P.H.S.; Surg. Reserve Div., Providence Hosp.; Field Lecturer and Demonstrator in Industrial Dermat., Div. Ind. Hygiene, Bur. State Services, U.S. Pub. Health Service; A.M.A.; F.A.A. Dermat. & Syph.; M., Soc. Invest. Dermat. & Syph.; Va. Acad. Sc.; Baltimore & Washington Dermat. Soc.; M., Assoc. Mil. Surgeons, U.S.

1940 **Garver, William Parrish,** Rose Bldg., Cleveland 14, Ohio.
b 1904. A.B., Cornell 1926; M.D., 1929; Sr. Vis. Phys. Med. and Vis. Allergy, Cleveland City Hosp.; Vis. Allergy, St. Vincent Charity Hosp.; Demonstr. Med. Western Reserve Med. Sch.; F.A.C.P., F.A.C.A.; M., Cleveland Allergy Soc.

1940 **Golan, Harry G.,** 104-34 Lefferts Blvd., Richmond Hills 19, N. Y.
b 1904. B.S., Coll. City N. Y. 1925; M.D., L. I. Med. Coll. 1929; Asst. Allergy Jewish Hosp. Brooklyn; Dir. Allergy, Wyckoff Heights Hospital, Brooklyn; A.M.A.

1942 **Gold, Herman,** 314 E. 9th St., Chester Pa.
b 1908. B.S., U. Pa. 1928; M.D., 1931; Assoc. Med. (Major Staff) Allerg., Chester Hosp.; M. Phila. Soc. Allergy.

1940 **Goldstein, Joseph D.,** 2801 Hudson Blvd., Jersey City, N. J.

1944 **Gottesman, James,** 315 East 17th St., New York, N. Y.
b 1903. B.S., N. Y. U. 1926; M.D., 1929; Asst. Adj. Allergy, Beth Israel Hosp.

1944 **Graham, William Randolph,** 201 West Franklin St., Richmond 20, Va.
b 1892. M.D., Med. Coll. Va. 1925; Cert. in Intern. Med. 1937; Vis. Phys., Johnston-Willis and Stuart Circle Hosps. and Retreat for the Sick; A.M.A.; M., South. Med. Assn.; Chairman, Sec. Allerg., 1942-1944.

1942 **Gray, Irving,** 25 Plaza St., Brooklyn 17, N. Y.
b 1892. M.D., U. of Bellevue Med. Sch. 1913; Lt. M.C., World War I; Cert. in Intern. Med. 1937 and in Gastroenterology 1943; Att. Phys. Coney Island Hosp.; Assoc. Att., Brooklyn Jewish Hosp.; Consult. Phys. Brooklyn State, Seaview, St. Joseph's, Far Rockaway, Long Beach, and Rockaway Beach Hosps.; F.A.C.P. and A.A. Indust. Phys.; M., A. Gastroenterol. Assn.; A. Pub. Health Assn.; A. Heart Assn.; N. Y. Acad. Med.; Nat. Tbc. Assn.; Assn. Adv. Indust. Med., Past Pres., 1941-1942; Past Pres., Second District Branch, N. Y. State Med. Soc., 1937-1938.

1941 **Green, Mayer A.,** 423 Jenkins Bldg., Pittsburgh 22, Pa.
b 1909. B.S., U. Pittsburgh 1929; M.D., 1932; Cert. in Intern. Med. 1941 and Allergy 1941; Allergy Dept., Montefiore Hosp.; A.M.A.; F.A.C.A.; M.A.C.P.

1940 **Greene, J. Evarts,** 263 Beacon St., Boston 16, Mass.

1942 **Greenhall, Armand L.,** 685 West End Ave., New York 25, N. Y.
b 1900. B.A., Columbia U. 1921; M.D., McGill U. 1927; Maj. M.C., Air Corps; Phys., Dept. Allergy, N. Y. and City Hosps., N. Y.; Neuropsychiatrist, N. Y. Post Grad. Hosp.; A.M.A.; M., Aero-Med. Assn.

1941 **Guild, B. Thurber,** 70-76 Laight St., New York 13, N. Y.
b 1885. M.D., Hahnemann Med. Coll. and Hosp. 1908; A.M.A.; M., Soc. Invest. Dermat.

1938 **Harris, Jesse S.,** 176 Dwight St., New Haven 11, Conn.
b 1895. B.A., Yale U. 1917; M.D., 1922; Att. Phys., New Haven Gen. and St. Raphaels' Hosps.; Phys. in charge, Allergy Clin., New Haven Hosp.; Asst. Clin. Prof. Med., Yale Med. Sch.; A.M.A.

1942 **Harris, Maurice Coleman,** 133 E. 58th St., New York 22, N. Y.
b 1899. Premed. Course, Tufts Coll., Boston; M.D., 1923; Comdr., M.C.-V(S), U.S.N.R.; Vis. Phys. and Chief, Allergy Clin., N. Y. Dispensary; Adj. Prof. Med. and Chief, Allergy Clin., N. Y. Polyclinic Hosp. and Post Grad. Med. Sch.; A.M.A.; F.A.C.P., N. Y. Acad. Med., and A.C.A.; M. Allergy Clinics Greater N. Y.; Soc. Adv. Allergy; Assn. Military Phys.; U. S. Naval Inst. (Assoc. Member); President, Audubon Med. Assn., 1936.

1940 **Harten, Max,** 135 Eastern Parkway, Brooklyn 17, N. Y.
b 1906. B.A., Columbia 1927; M.D., L. I. Coll. Med. 1934; Asst. Att. Allergy, Asst. Att. Chest, Jewish Hosp., Brooklyn; A.M.A.

1940 **High, Carl Milton,** 1532 N. 11th St., Reading, Pa.
b 1899. B.S., Ursinus Coll. 1924; M.D., Jefferson Med. Sch. 1928; Comdr., M.C., U.S.N.R.; Jefferson Hosp., Phila; Reading Hosp.; Berks Co. Tbc. Sanitorium; M., Phila. Allergy Soc.

1944 **Horn, Leonard,** 306 Laburnum Crescent, Rochester, N. Y.

1942 **Howes, Homer A.,** University of Michigan Hosp., Ann Arbor, Mich.

1940 **Hurwitz, George,** 84 Whiting Lane, W. Hartford, Conn.
b 1908. A.B., Harvard U. 1929; M.D., U. Md. 1933; Staff, Mt. Sinai and Hartford Hosps.; Capt., M.C., A.U.S.; Hartford Dispensary; A.M.A.

(To be continued.)